PSJ2 Exh 28

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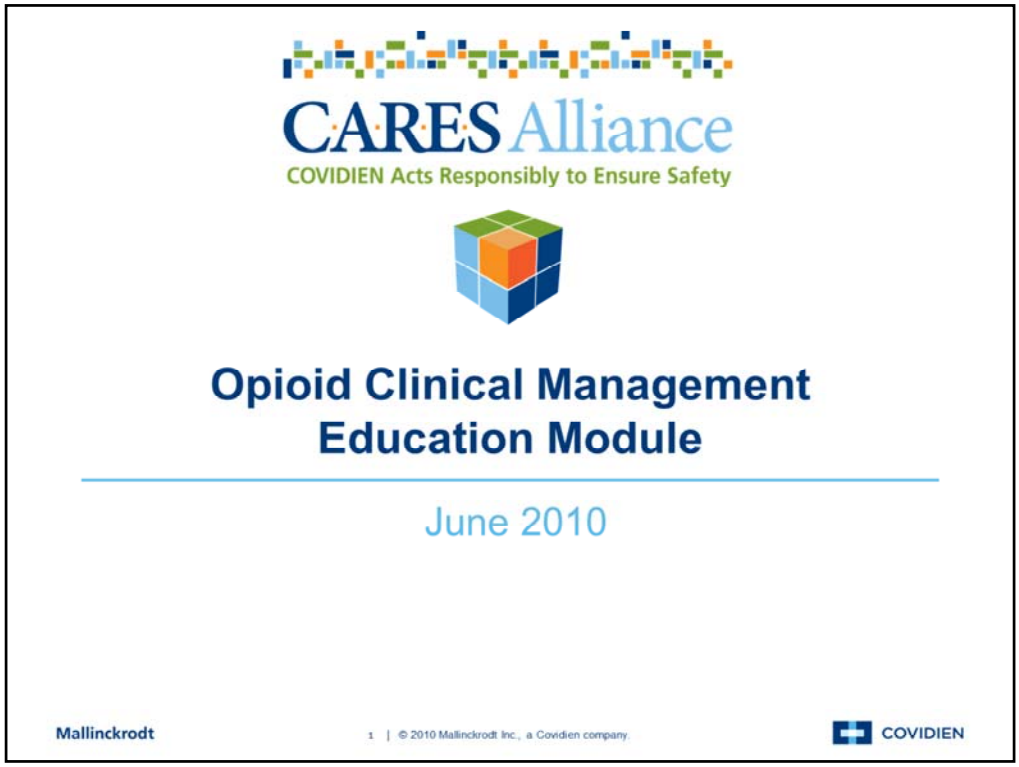
CARES Alliance
COVIDIEN Acts Responsibly to Ensure Safety
Opioid Clinical Management Education Module
June 2010
Mallinckrodt
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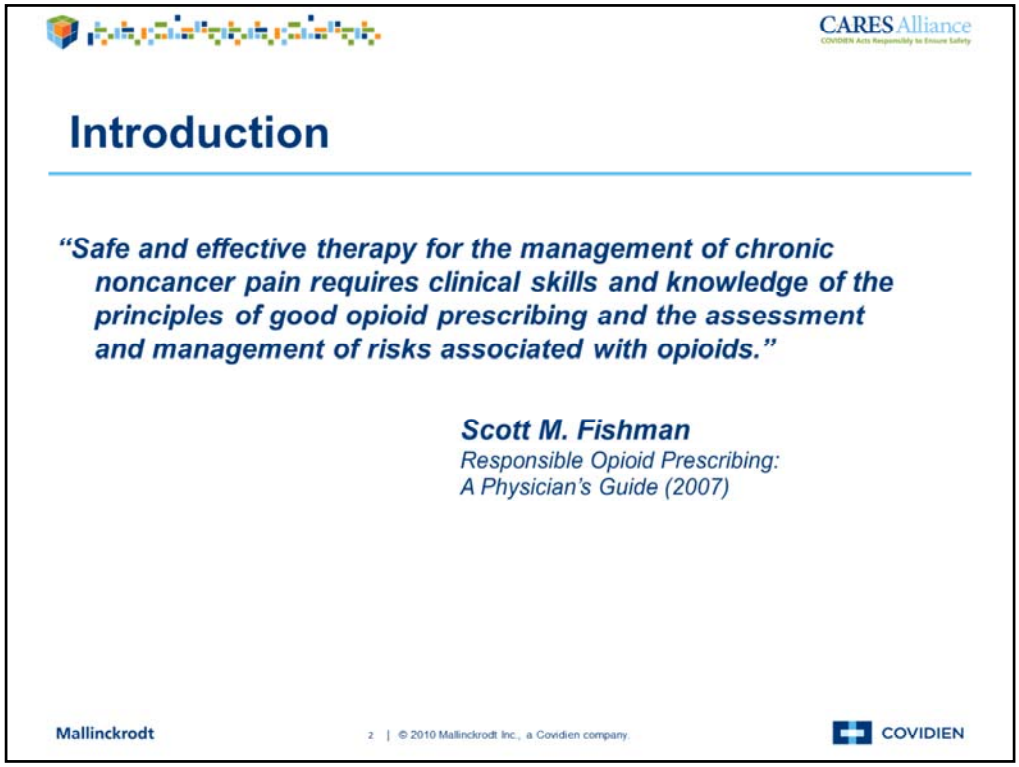
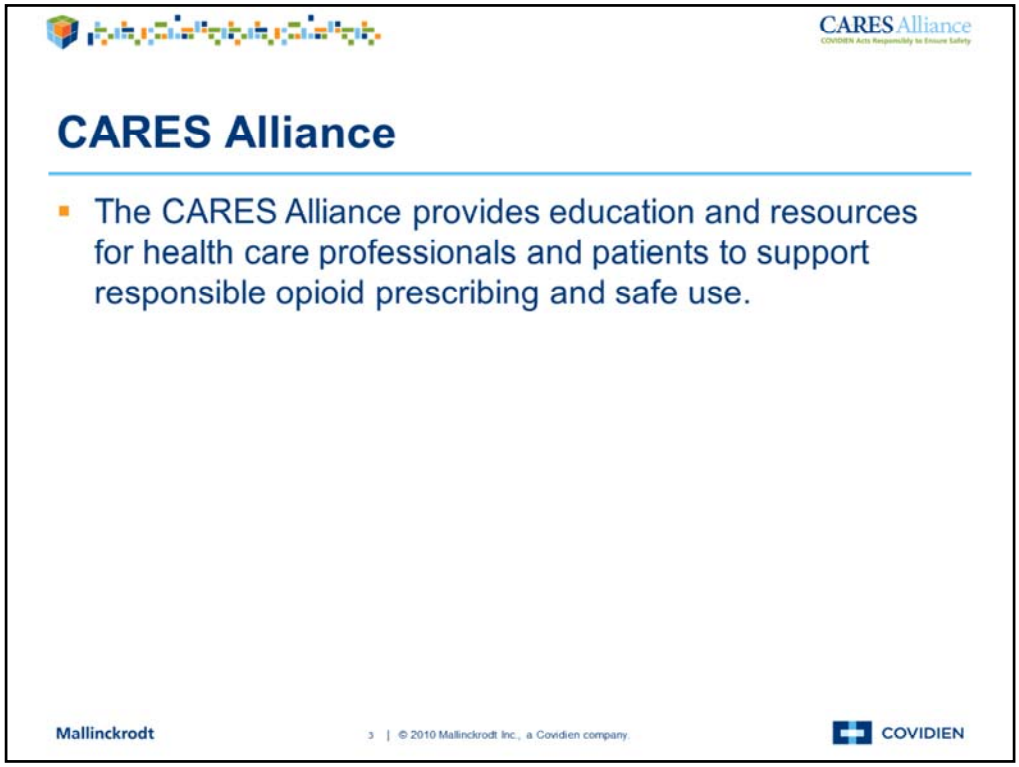
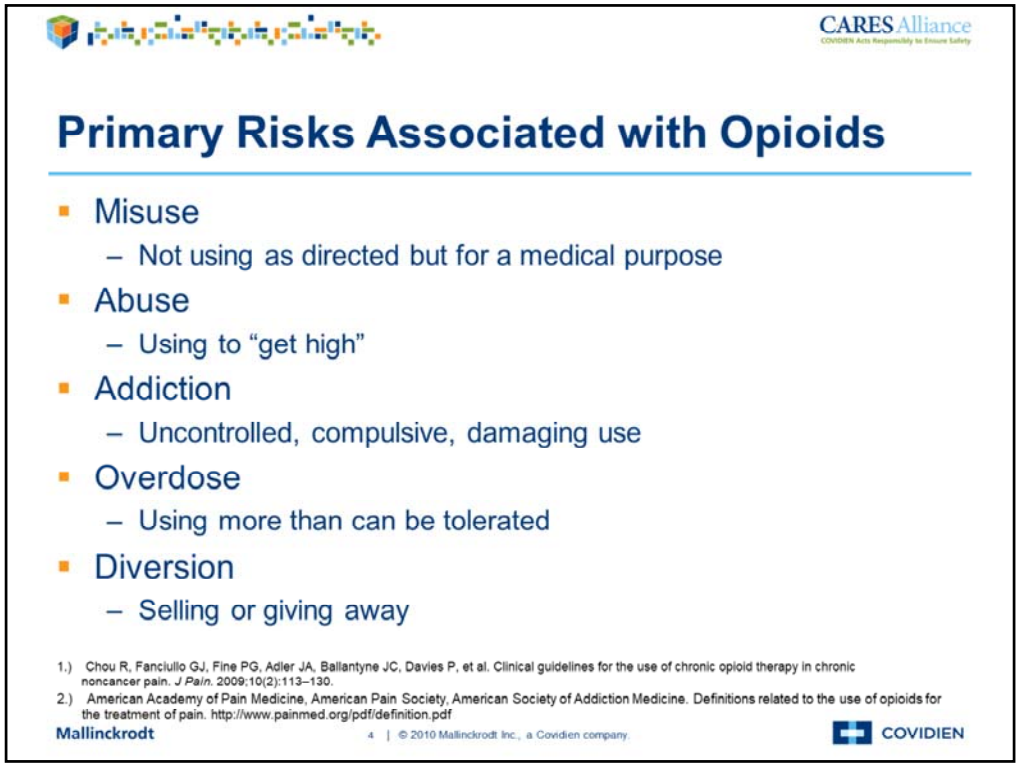


Safe and effective therapy for the management of chronic noncancer pain requires clinical skills and knowledge of the principles of good opioid prescribing and the assessment and management of risks associated with opioids. [Fishman/p8/¶3+Bullets–p9/Bullets]



The CARES Alliance provides education and resources for health care professionals and patients to support responsible opioid prescribing and safe use.



The risks associated with opioid use include:

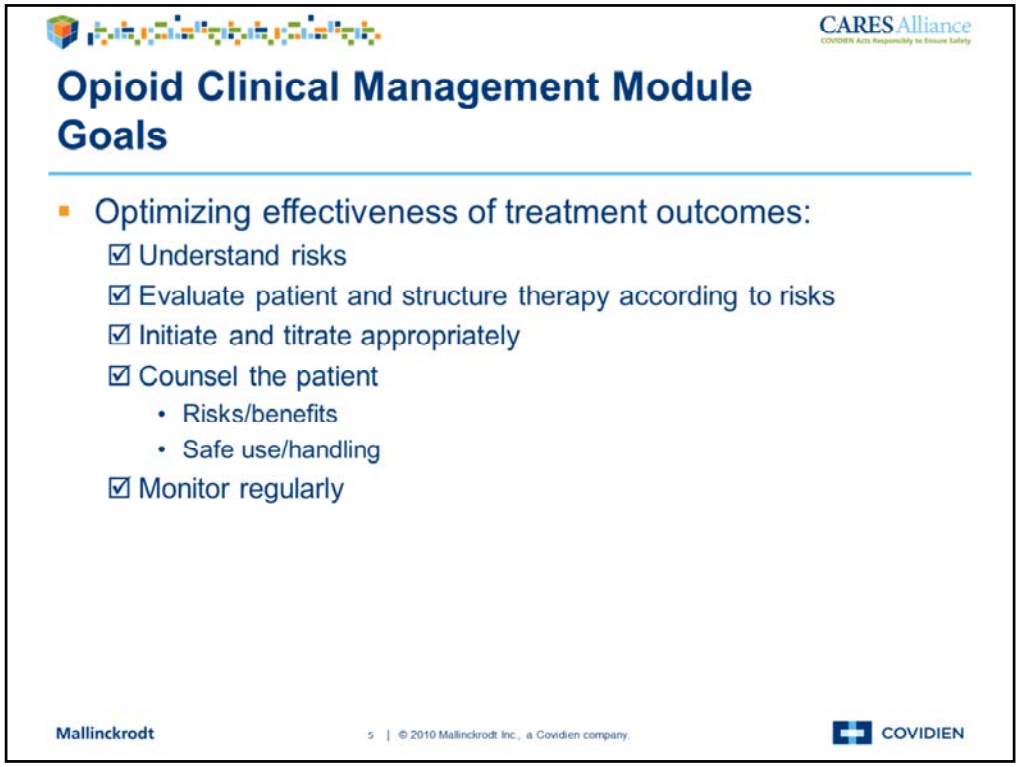
Misuse—use of a medication prescribed for a legitimate medical purpose other than as directed or indicated, whether willful or unintentional, and whether or not harm results [Chou/p130/Appendix B]

Abuse—use of a medication for a nonmedical purpose such as altering one's state of consciousness (eg, getting high) [Chou/p130/Appendix B]

Addiction—a neurobiologic disease characterized by impaired control over drug use, compulsive use, continued use despite harm, and craving [AAPM-APS-ASAM/p2/I]

Overdose—when larger quantities of a medication are taken than can be physically tolerated, resulting in serious, often harmful, and sometimes fatal toxic reactions, including central nervous system (CNS) and respiratory depression

Diversion—the intentional transfer of a controlled substance from legitimate distribution and dispensing channels [Chou/p130/Appendix B]



The Clinical Management Education Module summarizes years of experience by leading pain management and addiction medicine specialists and guidance from leading health care organizations.

The information provided in this presentation should help optimize the effectiveness of opioid analgesics and thereby improve patient outcomes in clinical practice by

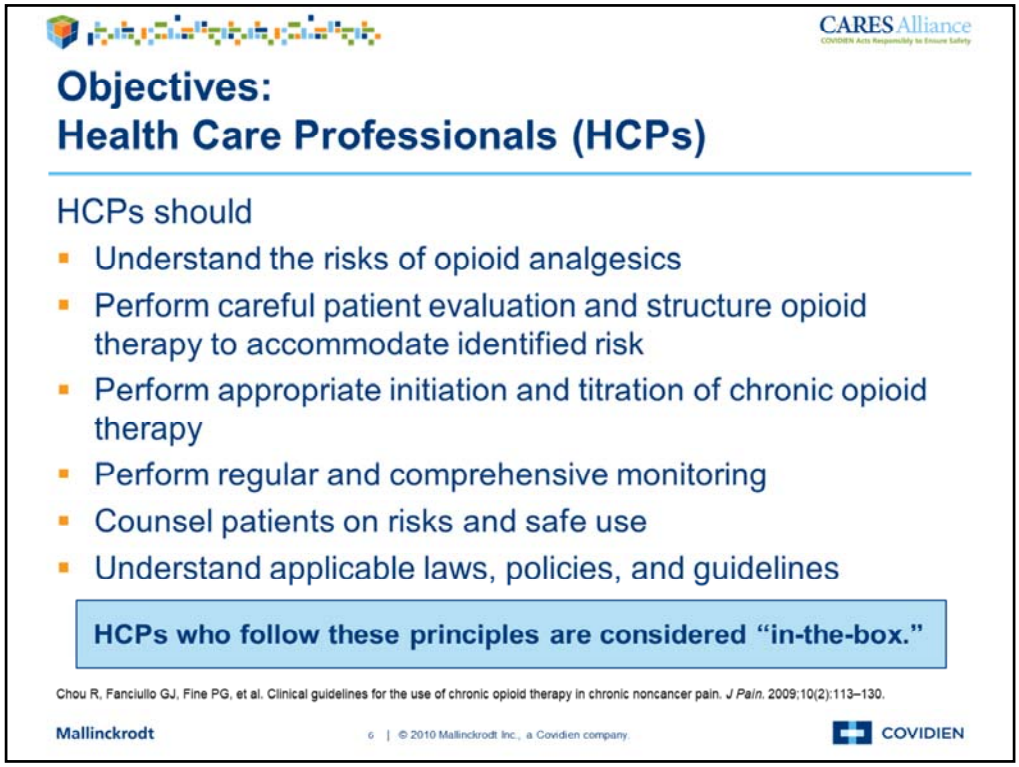
•Understanding the risks and potential adverse events associated with opioids

•Performing careful patient evaluation and structuring of opioid therapy to accommodate increased risk

•Appropriately initiating and titrating chronic opioid therapy

•Counseling patients on the risks and benefits of opioid therapy as well as on safe use and handling, including proper disposal

•Performing regular and comprehensive patient monitoring



Before and during prescribing opioid therapy to a patient, the HCP should understand the risks of opioid analgesics.

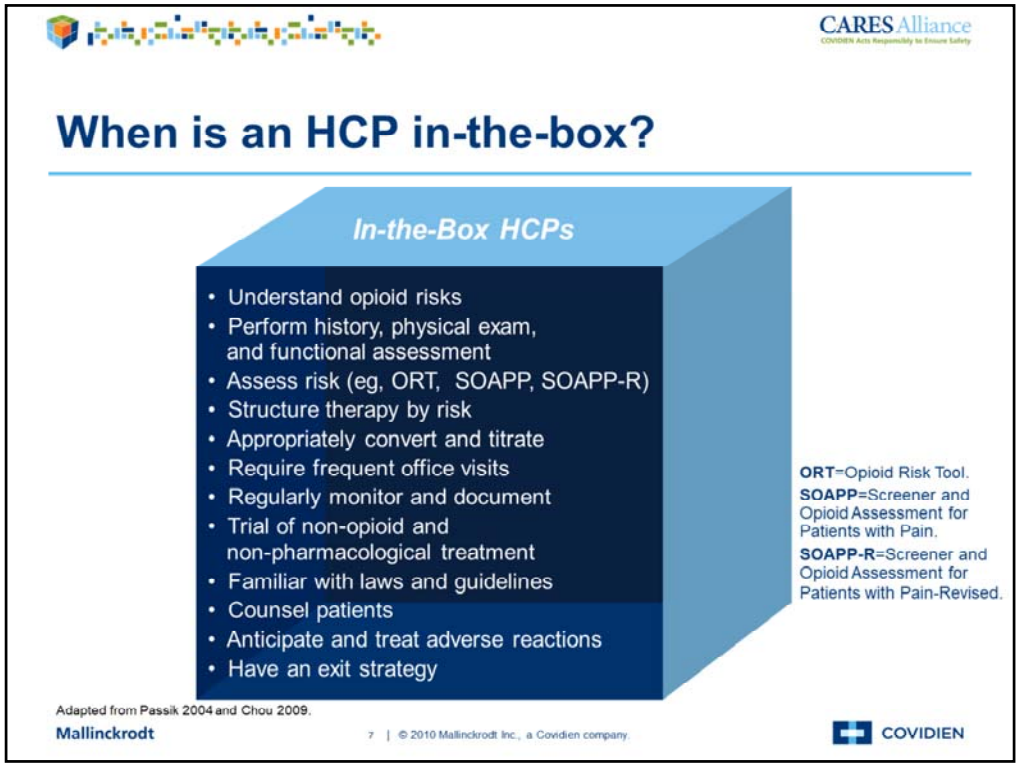
They should perform careful patient evaluation and structure opioid therapy to accommodate identified risk.

They should perform the appropriate initiation and titration of chronic opioid therapy, and should perform regular and comprehensive monitoring during treatment.

They should counsel patients on the risks associated with opioid therapy and the safe use of their medication.

And they should understand the applicable laws, policies, and guidelines.

Doing all this will put the HCP "in-the-box."



When is an HCP in-the-box?

In-the-box HCPs understand opioid risks. They perform a patient history, physical exam and functional assessment.

They assess patient risk using tools such as ORT and SOAPP-R.

They structure therapy by the identified risks.

They appropriately convert the patient if they are already taking a different opioid and titrate individually.

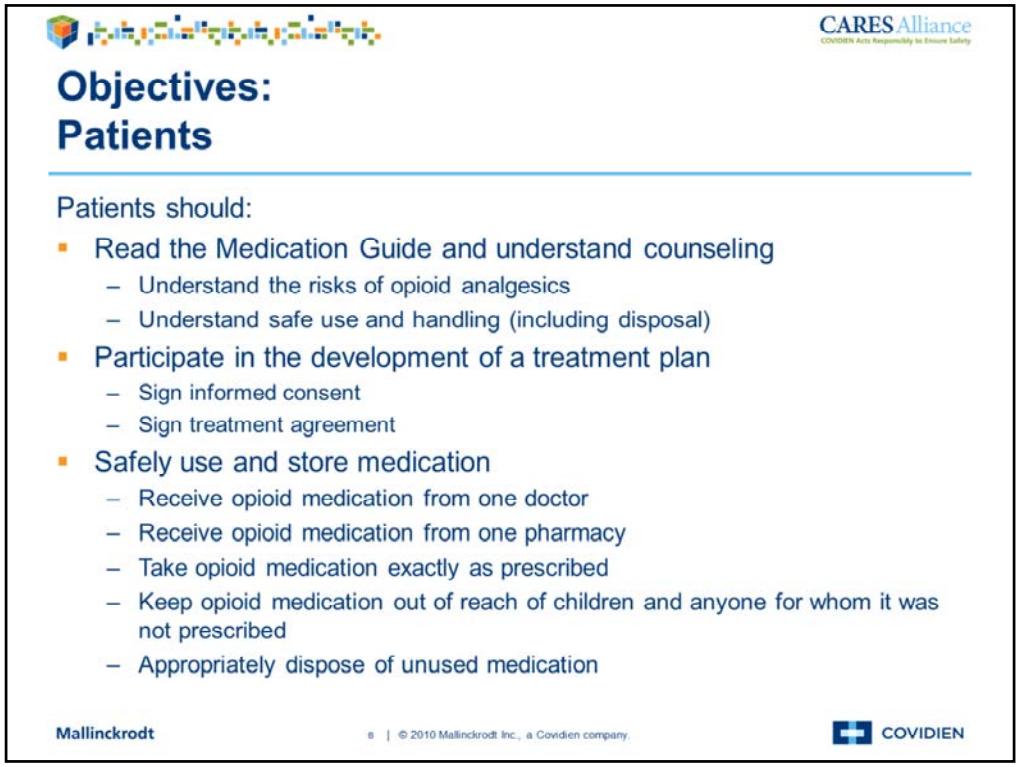
They require frequent office visits from the patient, and they regularly monitor and document treatment.

They offer and conduct trials of non-opioid therapy and non-pharmacological treatment.

They are familiar with the laws and guidelines pertaining to prescribing opioids.

They counsel patients, and anticipate and treat adverse reactions.

And finally, they have an exit strategy.



At the same time, patients considering opioid treatment have objectives they should meet.

Patients should read and understand the Medication Guide, including the risks of opioid analgesics and the safe use and handling of the medication (including how unneeded doses should be disposed).

They should participate in the development of a treatment plan, including signing informed consent and the treatment agreement itself.

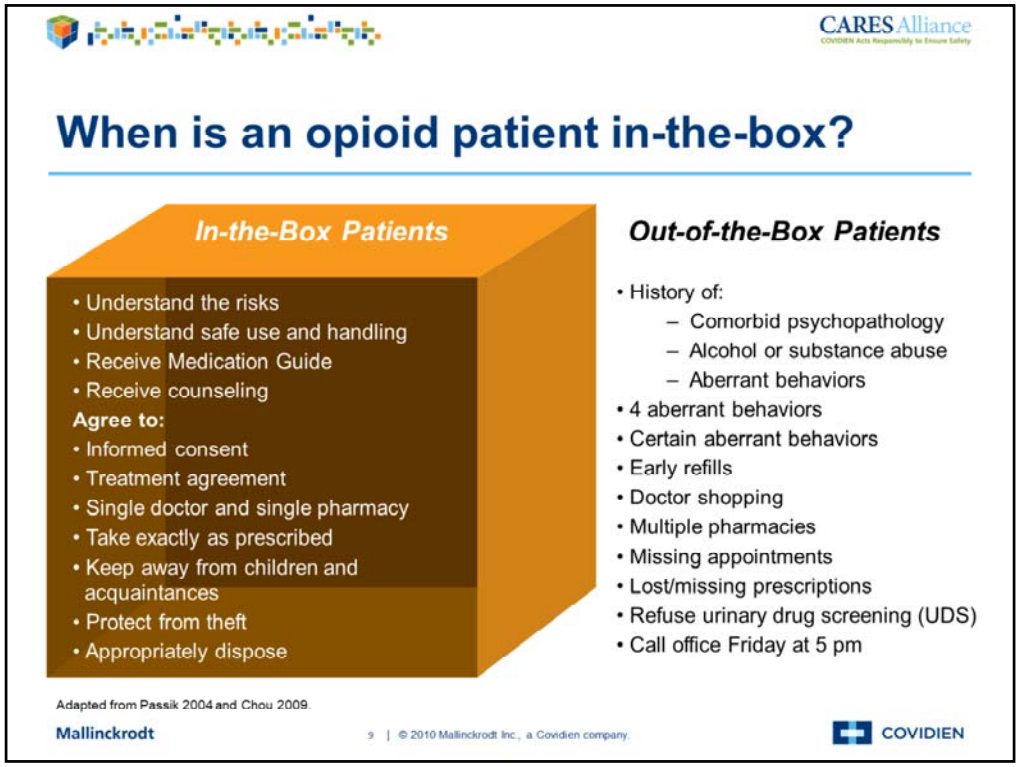
They should also safely use and store the medication while receiving therapy.

This includes receiving opioid medication from one doctor and from one pharmacy.

It includes taking opioid medication exactly as prescribed.

They must keep all opioid medications out of the reach of children and anyone for whom it was not prescribed.

And they should appropriately dispose of unused medication.



Just as an HCP should be in-the-box, so should the patient.

A patient is considered in-the-box when they understand the risks associated with opioid therapy and the safe use and handling of their medication.

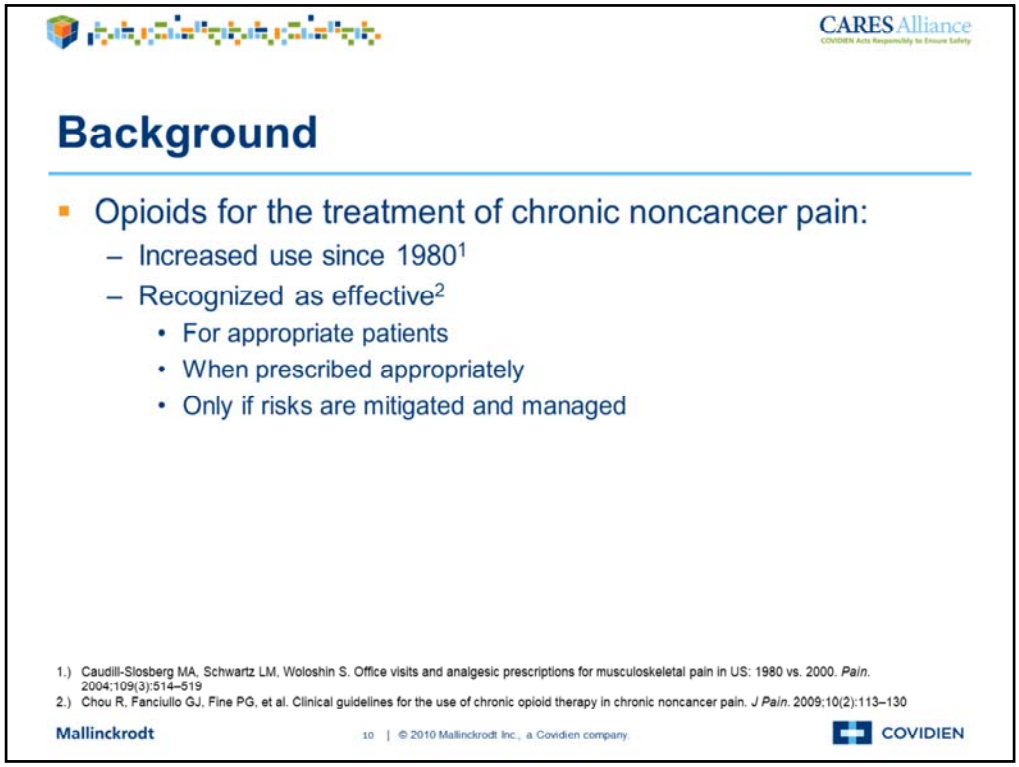
When they receive, read, and understand the Medication Guide and get counseling from their doctor.

When they agree to informed consent and the treatment agreement, use a single doctor and pharmacy, take their medication exactly as prescribed, keep their medication away from children and acquaintances, protect against the theft of their medication, and appropriately dispose of unneeded doses.

A patient may be considered out-of-the-box when they have a history of comorbid psychopathology, alcohol or substance abuse, or when they exhibit aberrant behaviors.

Also, they may be considered out-of-the-box if they have exhibited 4 aberrant behaviors or certain aberrant behaviors.

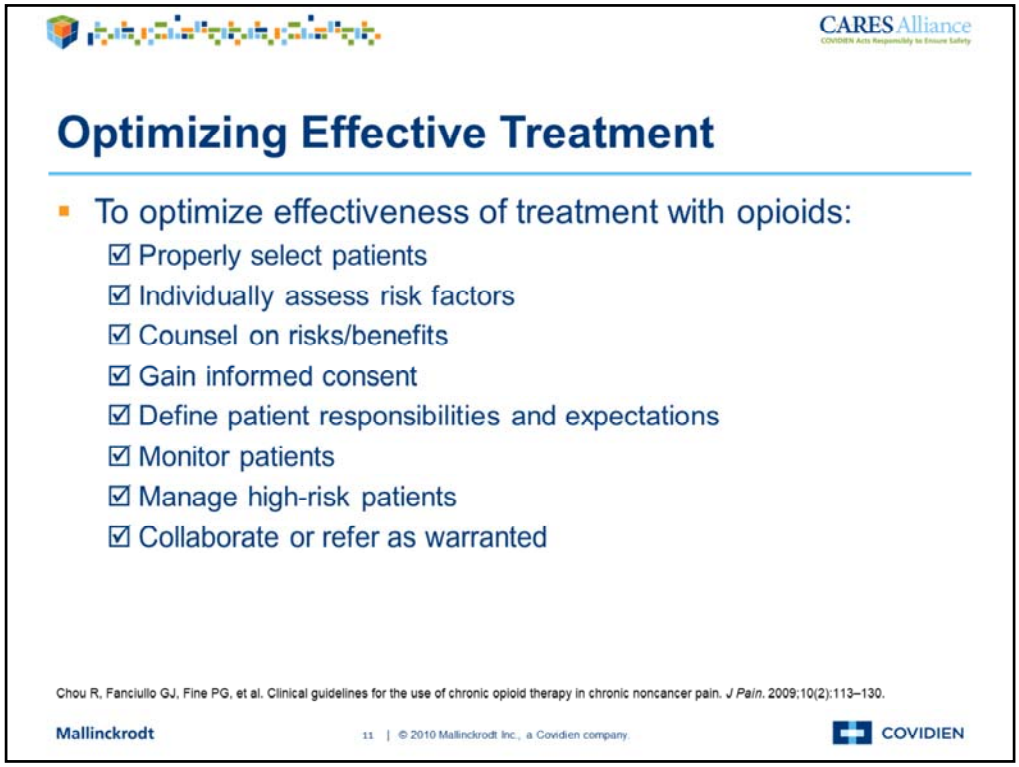
There are also certain aberrant behaviors that are more out-of-the-box such as if they request early refills, “doctor shop,” use multiple pharmacies, miss appointments, lose or misplace prescriptions, refuse UDS, or call the office Friday at 5 pm.



The use of opioid analgesics for the treatment of chronic noncancer pain has increased steadily since 1980. [Claudill-Slosberg/p1/¶1] [Olsen/p1/¶1]

Opioids are now recognized as effective therapy for select patients when prescribed judiciously and appropriately by HCPs who are knowledgeable of and skilled in assessing and managing the potential associated risks including misuse, abuse, addiction, overdose, and diversion.[Chou/p124/c1/¶1]

HCPs will encounter these risks in clinical practice when they prescribe opioids for their patients with chronic noncancer pain; 4%-10% of whom may have comorbid substance use or addictive disorders that must also be effectively managed.
[Gourlay/p108/c1/¶3;p109/c1/¶3]



HCPs can optimize the effectiveness of opioid analgesics in their practice by learning to:

•Properly select patients for opioid therapy by evaluating the benefits and risks [Chou/p115/c2/1.1]

•Stratify patients according to their individual risk profile for opioid abuse, misuse, and addiction [Chou/p115/c2/¶3]

•Counsel patients on the potential benefits and risks of opioid therapy [Chou/p116/c2/2.1]

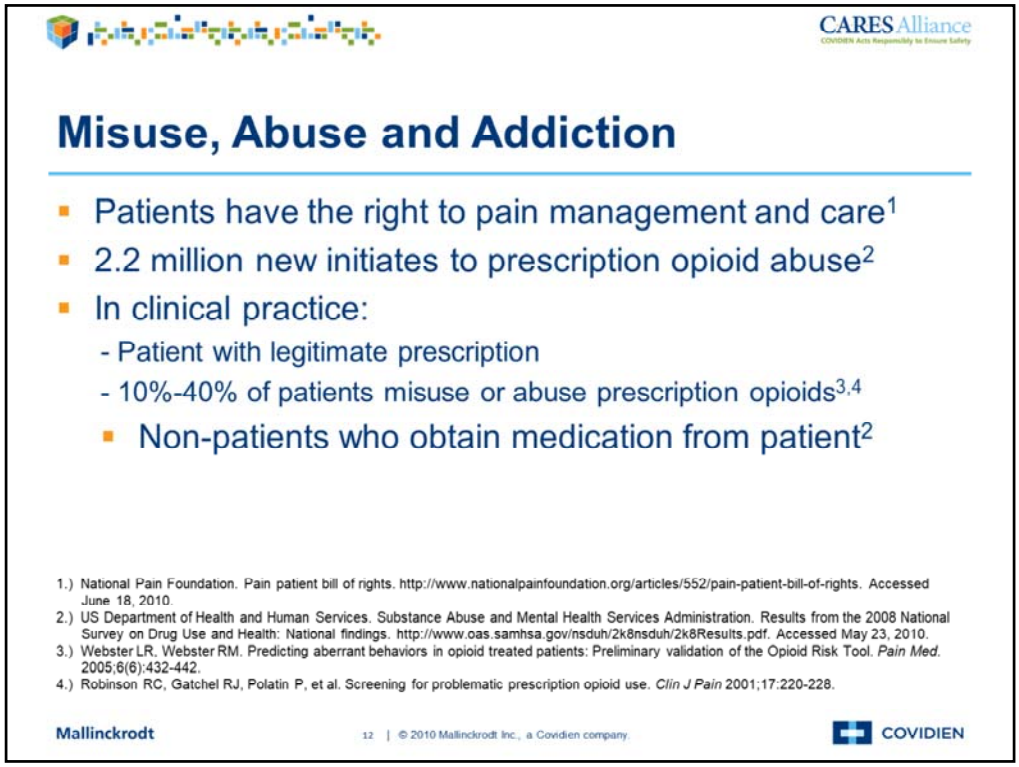
•Gain informed patient consent to opioid therapy with full knowledge of treatment goals, expectations, potential risks, and treatment alternatives [Chou/p116/c2/2.1]

•Define HCP and patient responsibilities and expectations using a written opioid use agreement [Chou/p116/c2/2.2]

•Monitor patients periodically and as warranted, including the use of UDS to confirm adherence to the prescribed opioid treatment plan [Chou/p118/c1–2/5.1+5.2]

•Manage patients who are at high risk for or who are currently engaging in aberrant drug-related behaviors, which are behaviors outside the boundaries of the agreed-on treatment plan.The treatment plan should be established as early as possible in the doctor-patient relationship. [Chou/p119/c1/6.1+6.2]

•Collaborate with or refer patients to specialists such as mental health or addiction specialists when needed. [Chou/p119/c1/6.1]

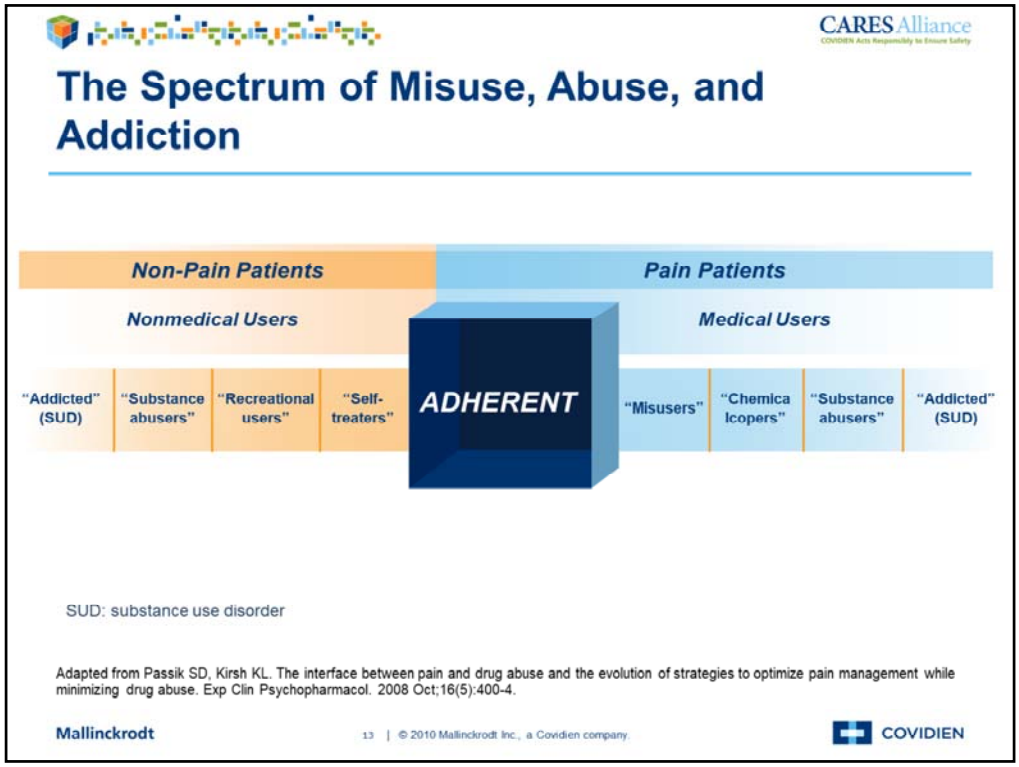


Patients have a right to proper, respectful, informed, and nondiscriminatory pain management and care. [NPF/p1/#1]

At the same time, as many as 10 – 40% of pain patients misuse or abuse prescription opioids. Prescription opioid abuse is common in non-patients as well. In 2008, 2.5 million over the age of 12 misused or abused prescription drugs for the first time. Of those, 2.2 million used pain relievers. [USDHHS/p57/Bullet 1]

All patients treated with opioids should be carefully monitored for signs of abuse and addiction. HCPs should also be aware that in clinical practice, abuse of prescription opioids comes primarily through legitimate prescriptions from a single prescriber.

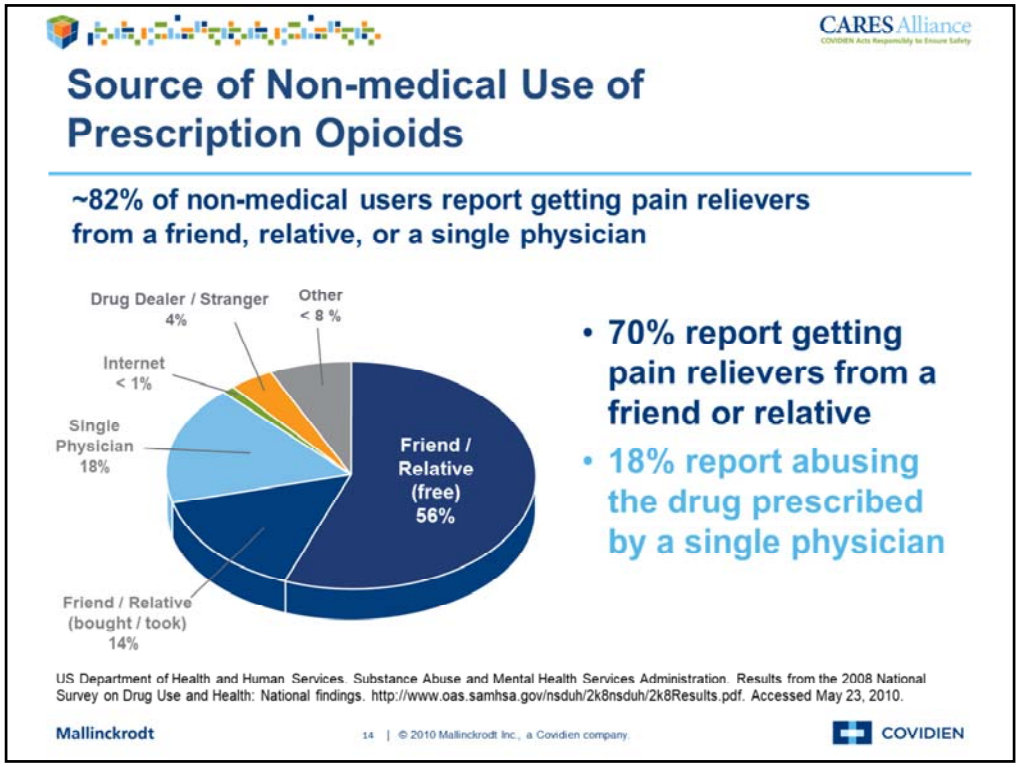
Prescription opioids may be misused or abused by the patients to whom they are prescribed for legitimate medical purposes or by others who typically obtain opioids from patients with a legitimate prescription. [USDHHS/p30/¶2+3]



HCPs should be aware of the spectrum of misuse, abuse, and addiction. The spectrum is different for pain patients vs. non-pain patients.

Some non-pain patients use prescription opioids to treat symptoms such as pain while others use prescription opioids recreationally to get high. Others still, are further along the spectrum of more severe and consistent substance abuse or addiction.

The spectrum of non-adherence in pain patients can be very complex. While the majority of patients may be strictly adherent, some misuse their prescription opioids by taking them other than as directed or indicated for a medical purpose. Others still, may abuse their prescription opioids to chemically cope or may be further along the spectrum of more severe and consistent substance abuse or addiction.

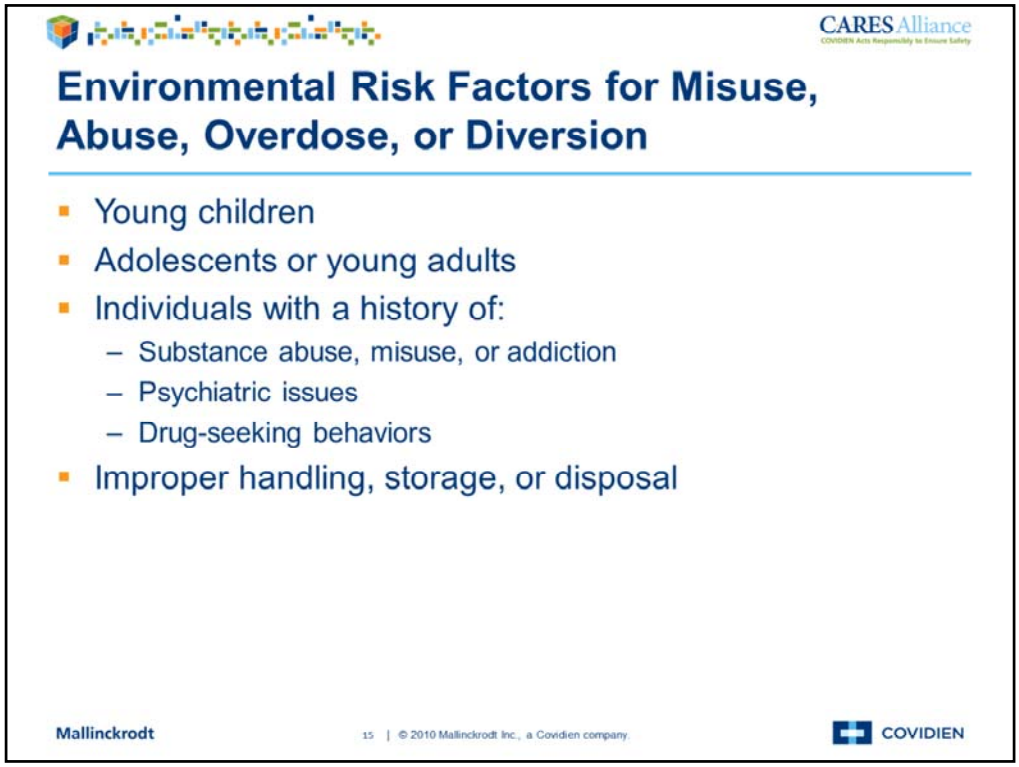


For adults 26 or older, prescription drug abuse (1.9%) is the most common illicitly used drug behind only marijuana (4.2%).[USDHHS/21]

70% of those who abuse prescription pain relievers get them from a friend or relative. [USDHHS/p30]

18% of patients who abuse prescription drugs obtain them legitimately from their HCP. [USDHHS/p30]

Therefore nearly 90% of prescription opioid abuse comes from a friend, relative, or single health care provider. Health care providers who prescribe opioid analgesics can unwittingly be at the head of the supply chain for opioid abuse and, therefore, have an opportunity to break the chain of abuse.



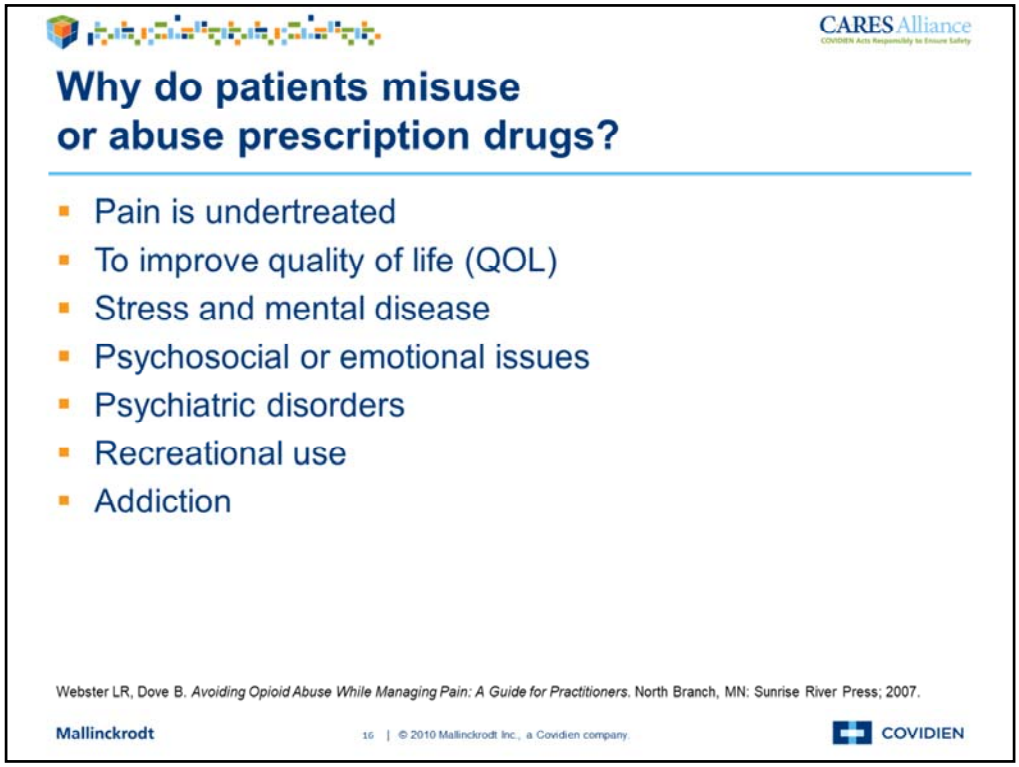
In addition to the individual risk factors for prescription drug abuse, a patient may possess, environmental risk factors exist as well.

These include:

•Having young children, adolescents or young adults living in or regularly visiting the patient's home

•Having individuals with a history of substance abuse, misuse or addiction, psychiatric issues, or drug-seeking behaviors living in or regularly visiting the patient's home

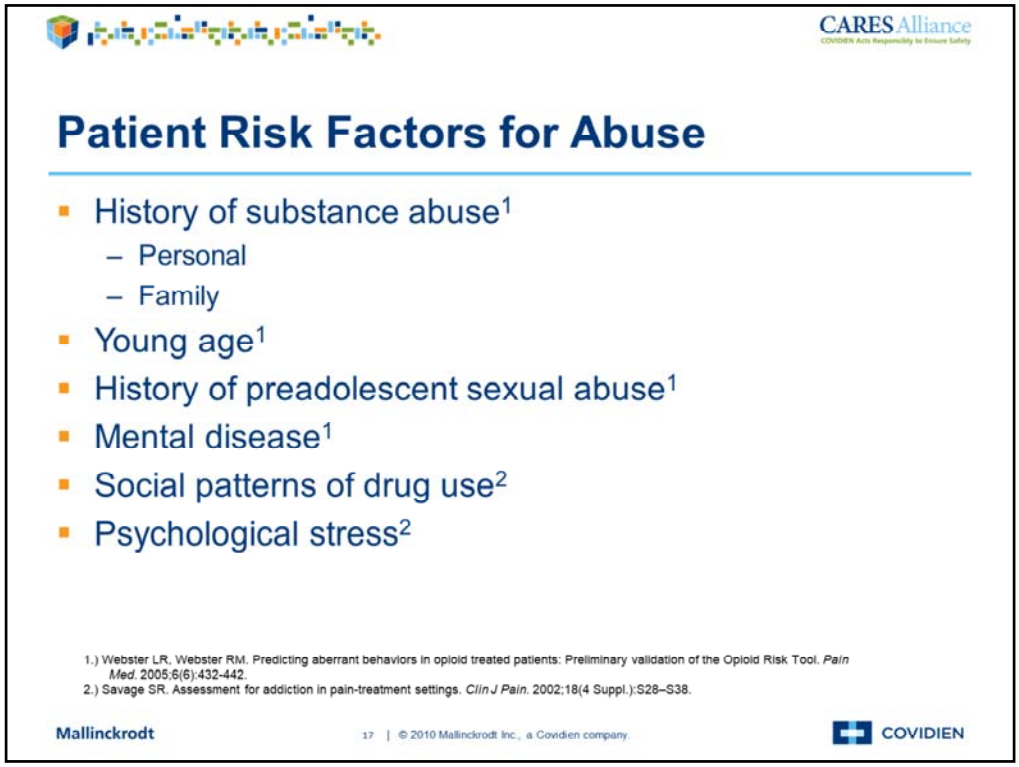
•Improper medication handling, storage, or disposal by the patient or caregiver



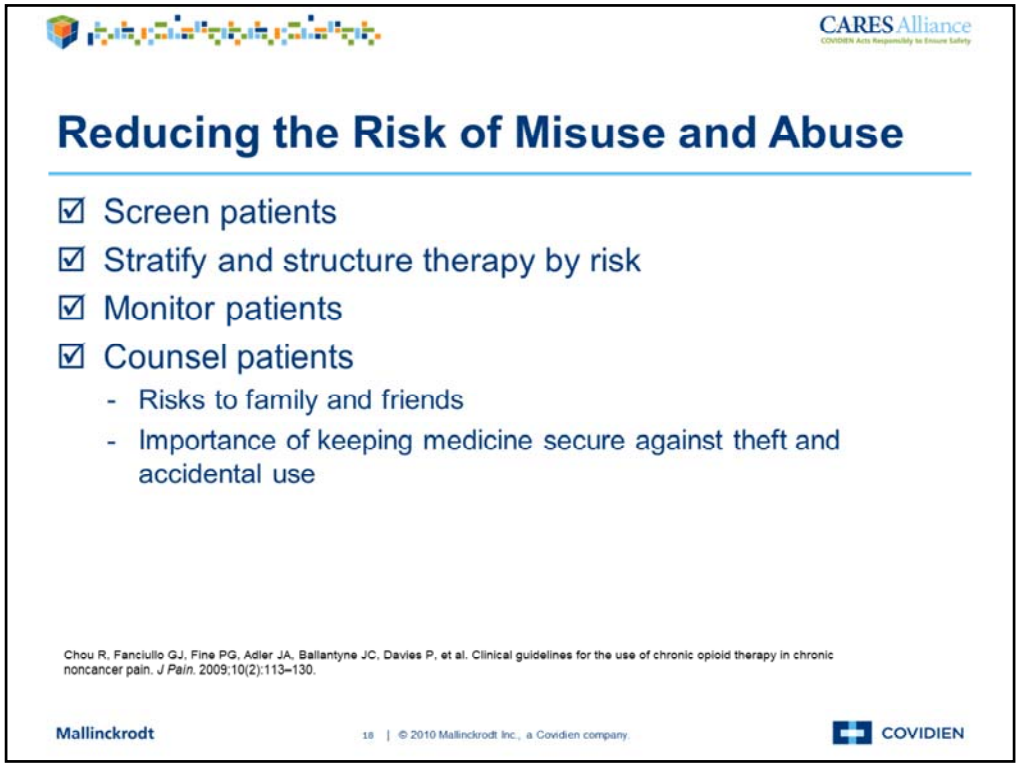
Patients with pain who misuse or abuse prescription opioids identify the following reasons for their misuse or abuse: [Webster 2007/p24/Abuse]

- Uncontrolled pain (drug-seeking behavior as a result of undertreatment)
- Rational misuse (intentional misuse to improve function and QOL)
- Chemical coping (intentional misuse as a result of stress or mental disease)
- Psychosocial or emotional issues
- Psychiatric disorders
- Recreational use (eg, use with illicit stimulants)
- Addiction

These reasons provide a roadmap for HCPs to proactively intervene with patient counseling and education.



Research has identified several known risk factors for abuse of prescription opioids, including: A personal or family history of substance abuse; younger age; and a history of preadolescent sexual abuse, especially in women. Additional risk factors for abuse include a history of current mental disorder such as anxiety and social patterns of drug use. Finally, psychological stress, whether acute or chronic, can increase the risk of abuse in patients.



To reduce the risk of patient misuse and abuse of opioids, HCPs can:

1) Screen patients for risk of misuse, abuse, and addiction

Tools that may help in stratifying risk include: Screener and Opioid Assessment for Patients with Pain (SOAPP), the Opioid Risk Tool (ORT), and the Diagnosis, Intractability, Risk, Efficacy (DIRE). [Chou/p114/c2/¶2]

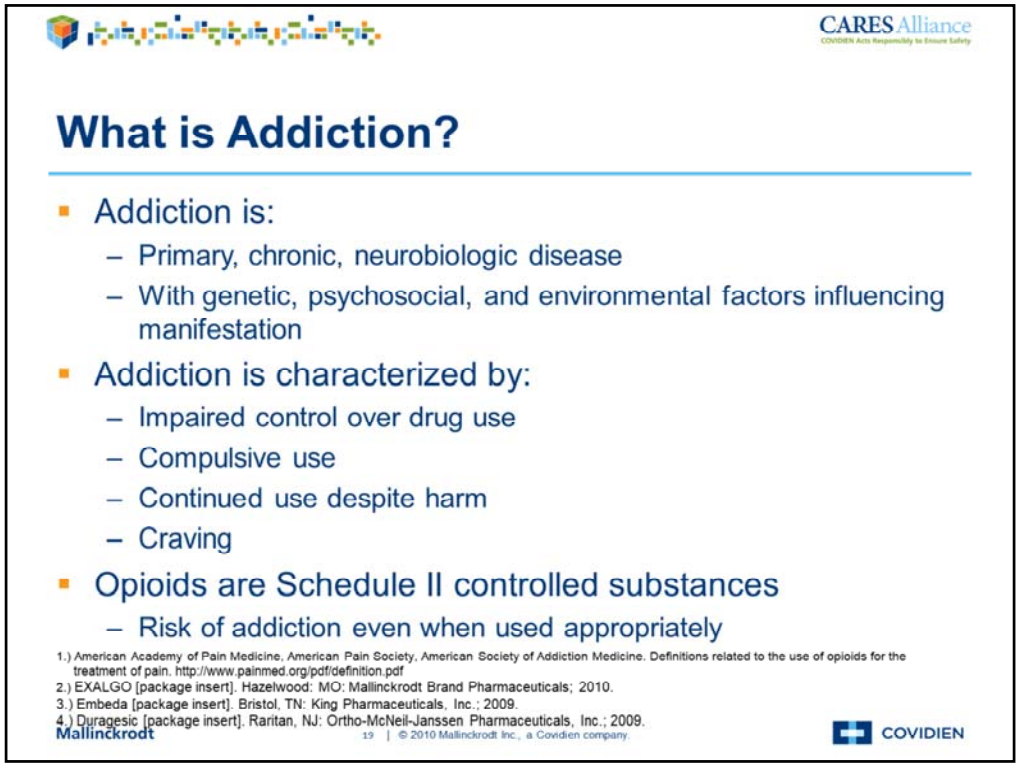
2) Stratify treatment for risk of misuse, abuse, and addiction

This can be used as a practical framework to help determine which patients may be safely managed in the primary care setting, those who should be comanaged in the primary care setting, those who should be comanaged with specialist support, and those who should be referred on for management of their chronic pain condition in a specialist setting.

3) Regularly monitor patients for changes in potential risk factors, including aberrant drug-related behaviors and UDS

Risk stratification can help determine the level of monitoring necessary, including how often UDS is recommended.[Chou/p118/c1-2/5.1+5.2]

4) Counsel patients on the risks to family, friends, and household acquaintances of opioid misuse, abuse, overdose, and diversion, as well as on the importance of keeping prescription opioids secure against theft and accidental use[Chou/p115/c2/1.1+¶3; p116/c2/2.1+2.2; p117/c1–2/3.1+3.2; p118/c1–2/5.1+5.2; p119/c1/6.1+6.2]



Overall cost in the US of drug abuse annually is estimated to be 0.5 trillion dollars. [NIDA: Info Facts. June 2008]

Addiction is a primary, chronic, neurobiologic disease with genetic, psychosocial, and environmental factors influencing its development and manifestation.

Use of opioid analgesics carries the risk of addiction even under appropriate medical use. [Chou/p124/c1/¶1]

Addiction is characterized by behaviors that include 1 or more of the following:

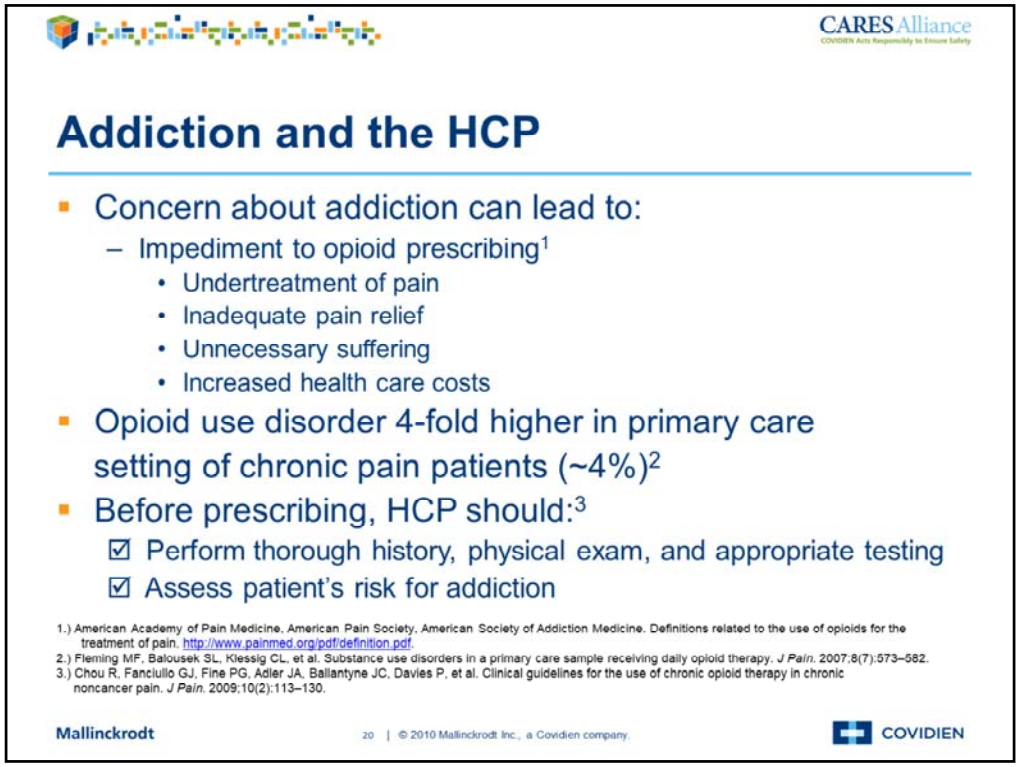
1) Impaired control over drug use

2) Compulsive use

3) Continued use despite harm, and

4) Craving

Opioids prescribed for the treatment of chronic pain are Schedule II controlled substances, which can be abused and may lead to addiction.

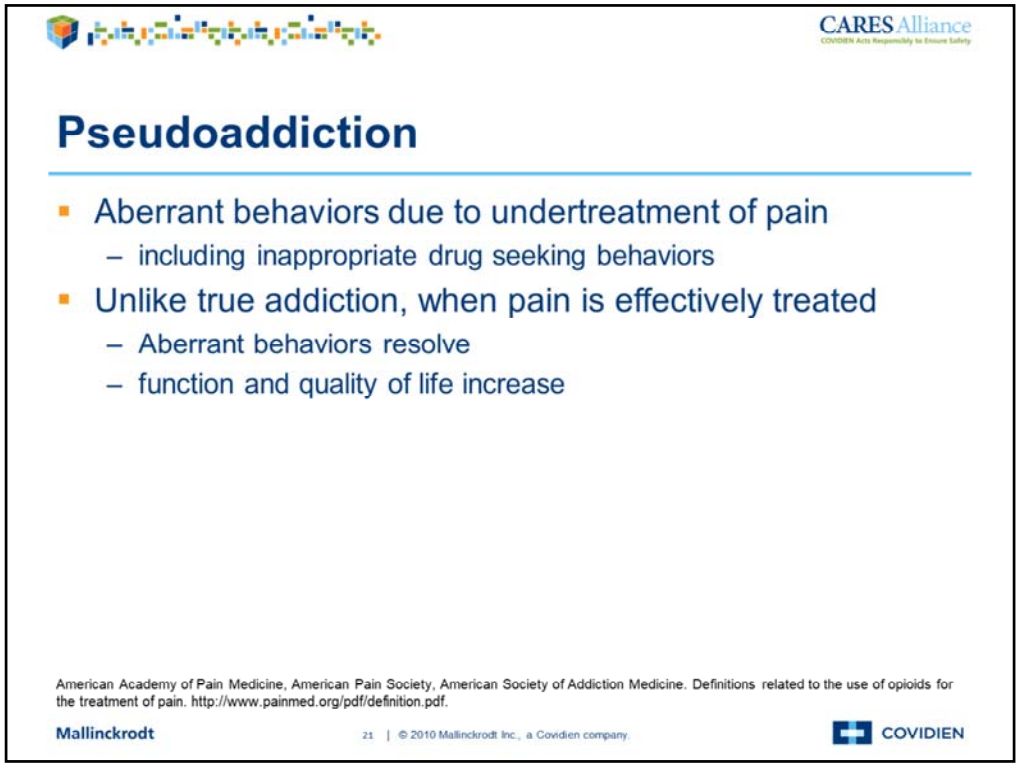


Concern about addiction can be an impediment to opioid prescribing and use, resulting in undertreatment of pain, inadequate pain relief, unnecessary suffering, and increased health care costs. [AAPM-APS/p1/¶2]

However, a study of patients with chronic pain being treated with opioid analgesics in the primary care setting found that the rate of opioid use disorders was 4-fold higher than in the general population (3.8% versus 0.9%). [Fleming/p579/c2/¶4]

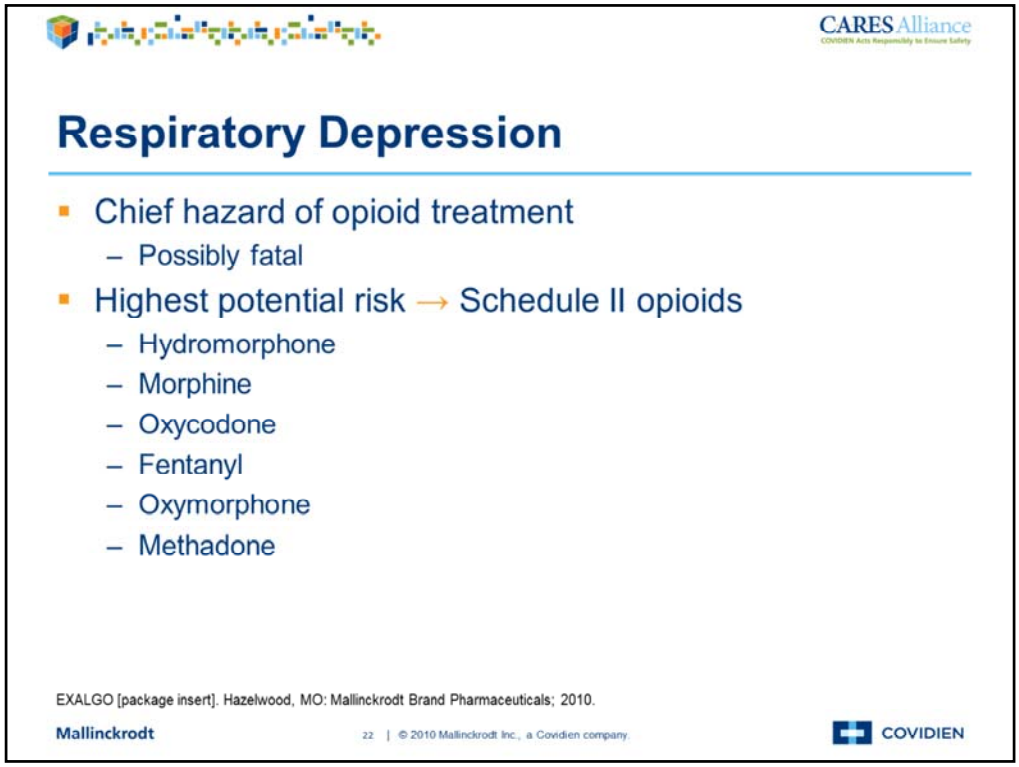
It is vitally important, therefore, that HCPs understand the potential risks associated with opioid analgesics, and know how to properly prescribe opioids and counsel patients on their safe use. [FSMB/p2/¶7]

Before prescribing opioid analgesics for chronic pain, HCPs should perform a thorough history, physical examination and appropriate testing, and assess the patient's risk for addiction. [Chou/p115/c2/1.1]



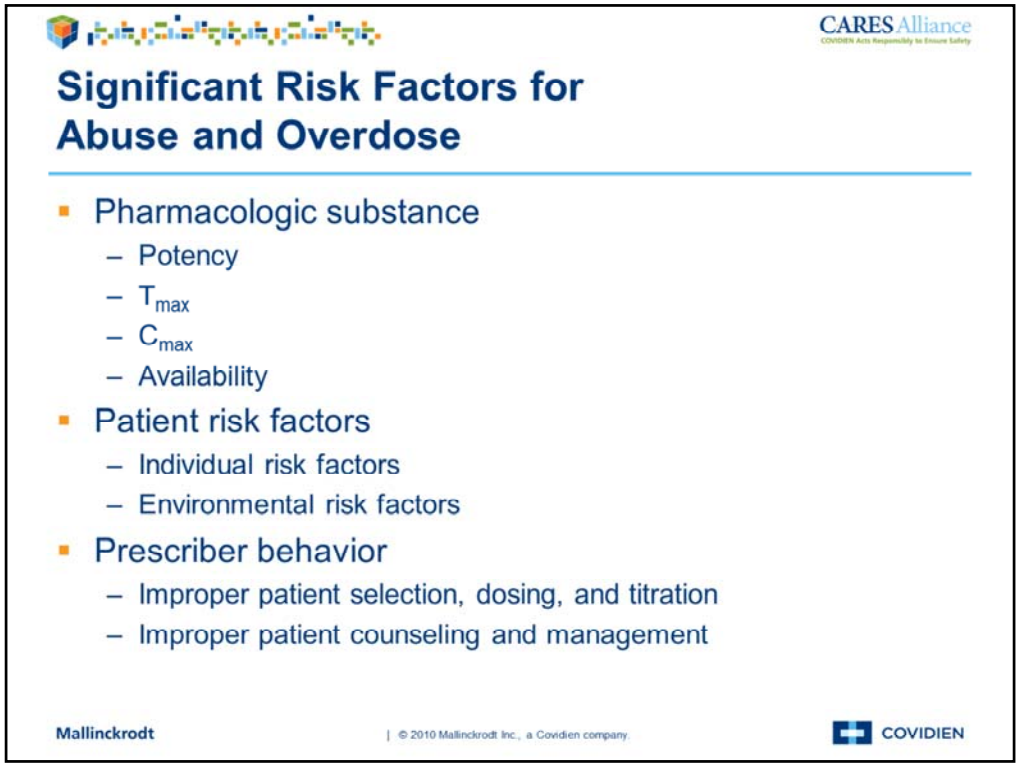
Some patients may exhibit aberrant behaviors, including inappropriate drug seeking behaviors when pain is undertreated.

Unlike true addiction, however, these behaviors resolve, and function and quality of life increase, when pain is effectively treated



Respiratory depression is a chief hazard of opioids and may occur in patients who are not opioid tolerant or who take too high an opioid dose. [EXALGO PI/p3/¶1] [Embeda PI/p6/c2/10.1] [Opana PI/p18/¶2] [Oxycontin PI/p20/¶8] [Duragesic PI/p5/c1/¶9]

In fact, Schedule II opioids, including hydromorphone, morphine, oxycodone, fentanyl, oxymorphone, and methadone have the highest potential risk of fatal overdose due to respiratory depression. [EXALGO PI/p3/¶1]

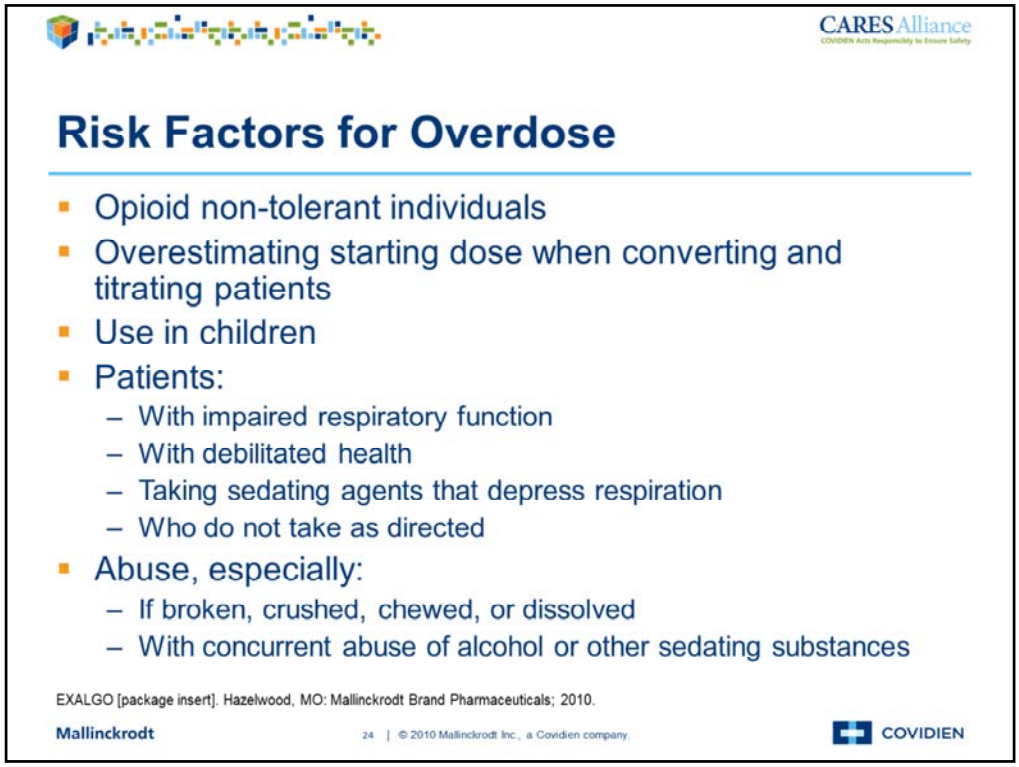


There are several key factors that affect a given product's risk of abuse.

T_{max}, or the speed at which a given substance reaches maximum plasma concentrations and C_{max}, or the maximum plasma concentration, are characteristics of a drug that can affect its abuse liability. However, the availability of a given drug is also a very important risk factor for abuse.

Certain patients are at greater risk of opioid abuse, overdose, and addiction based upon their individual or environmental risk factors. Knowing a patient's individual and environmental risk factors is an important part of risk assessment and stratification as well as structuring of treatment including monitoring.

Prescriber knowledge, attitude, behavior, and skills are critical for recognition and mitigation of the risks of abuse and overdose.



Overdose is another serious risk associated with opioid treatment.

Risk factors for overdose:

•Use in patients who are not opioid tolerant and already taking the equivalent of 60 to 100 mg of morphine daily or 50 to 300 mg transdermal fentanyl per hour.

•Overestimating the dose when converting patients from another opioid medication or titrating patients too quickly to allow sufficient time for blood levels to reach steady state. [EXALGO PI/p4/¶8] [Duragesic PI/p5/c1/¶18]

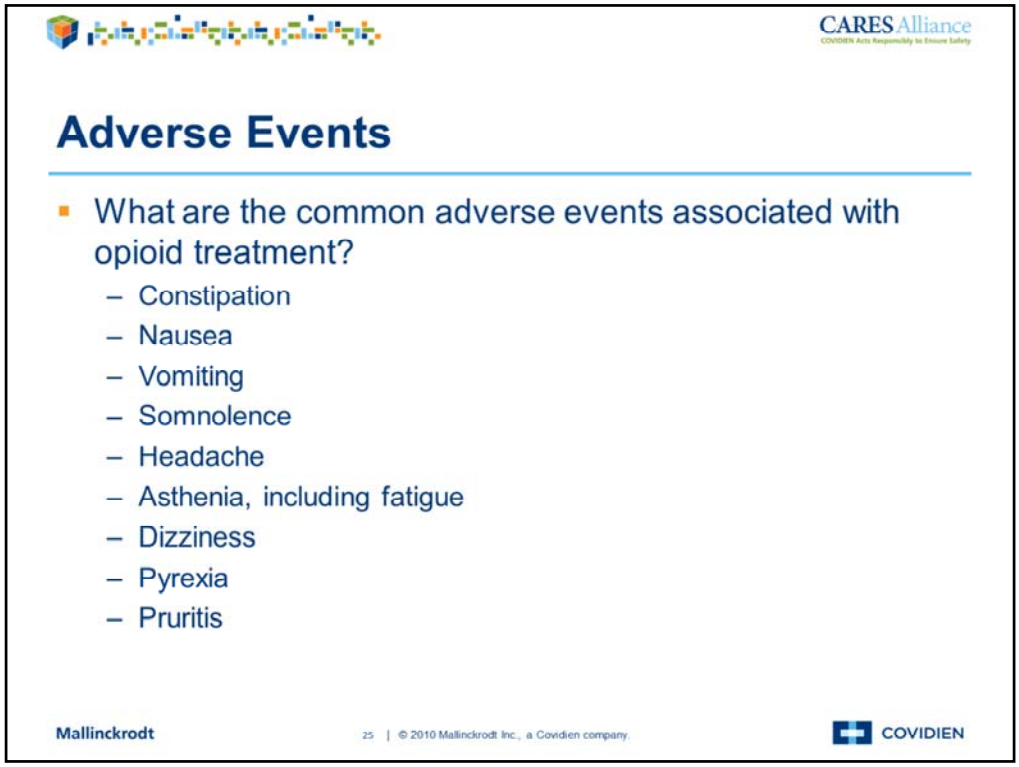
•Accidental consumption by children. [EXALGO PI/p1/c1/Bullet 5] [Embeda PI/p9/c1/Bullet 8] [Opana PI/p12/12] [Oxycontin PI/p28/Bullet 5] [Duragesic PI/p3/c2/¶1]

•Use by anyone for whom they were not prescribed.

•Taking opioids concomitantly with alcohol. [EXALGO PI/p9/¶5] [Embeda PI/p2/c1/¶5;p3/c1/¶19–c2/¶1] [Oxycontin PI/p10/¶9] [Opana PI/p8/¶5] [Duragesic PI/p3/c1/¶18]

•Altering the recommended administration of opioid analgesics, such as by breaking, chewing, dissolving or crushing tablets, by snorting, injecting or inhaling ingredients meant to be swallowed whole, or by taking a transdermal opioid orally, [EXALGO PI/p1/c1/Bullet 6] [Embeda PI/p1/c1/Bullet 2] [Opana PI/p8/¶2] [Oxycontin PI/p20/¶9] [Duragesic PI/p3/c1/¶4] as this may lead to rapid release and absorption of a potentially fatal opioid dose. [EXALGO PI/p1/c1/Bullet 6] [Embeda PI/p1/c1/Bullet 2] [Opana PI/p8/¶2] [Oxycontin PI/p20/¶9] [Duragesic PI/p3/c1/¶4]

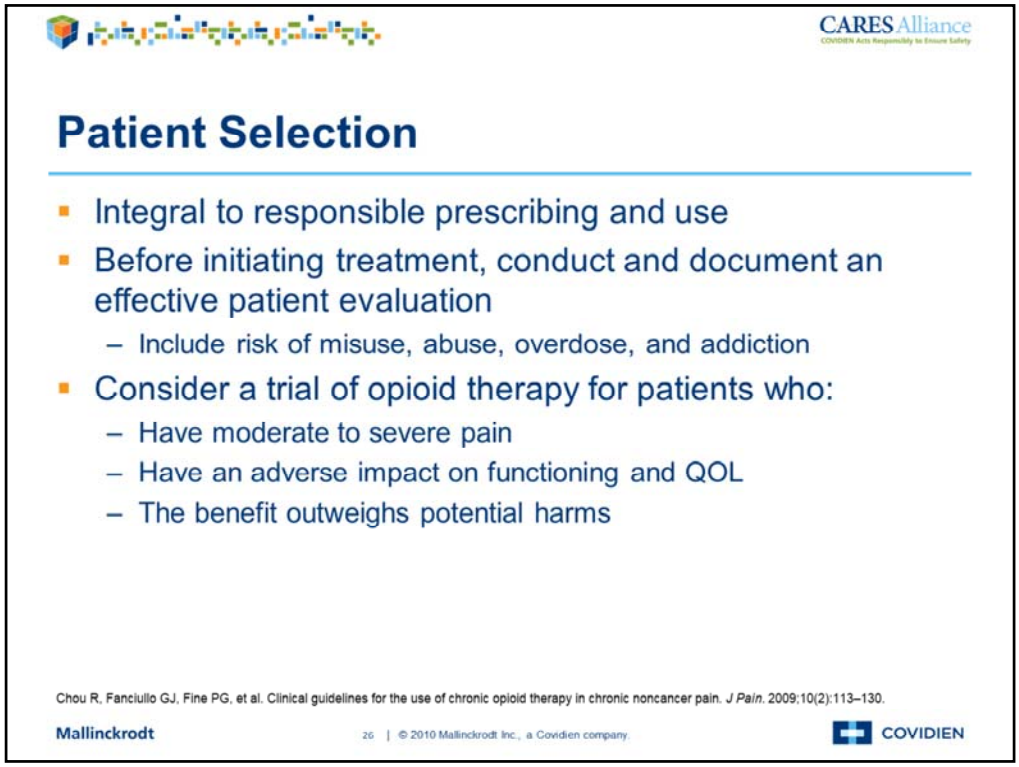
•Taking opioids with other CNS depressants. [EXALGO PI/p9/¶5] [Embeda PI/p2/c1/¶5;p3/c1/¶19–c2/¶1] [Oxycontin PI/p10/¶9] [Opana PI/p8/¶5] [Duragesic PI/p3/c1/¶18]



The most common adverse events associated with oral opioid analgesics occurring in >10% of patients are gastrointestinal (GI)- and CNS-related.

HCPs should anticipate, identify, and treat common opioid-associated adverse effects. [Chou/p121/c1/8.1]

Adverse events are another risk commonly associated with opioid therapy and can therefore be anticipated and either treated prophylactically or managed if they occur.



Patient selection is an invaluable tool to help mitigate the risks associated with opioid treatment. An important factor in selecting patients for opioid therapy is opioid tolerance. Many opioid analgesics, and high doses of most opioid analgesics, should only be prescribed for patients who are already opioid tolerant. [EXALGO PI/p3/¶3] [Embeda PI/p1/c1/Bullet 4] [Oxycontin PI/p1/¶5] [Duragesic PI/p1/c1/¶3]

HCPs may consider a trial of opioid therapy in patients whose pain is moderate to severe, who are having an adverse impact on function or quality of life, and in whom the potential therapeutic benefits outweigh the potential harms. [Chou/p115/c2/1.2]

Before initiating treatment, HCPs should conduct, and document in the medical record, a thorough patient history, physical examination, and appropriate testing including assessment of risk of substance abuse, misuse, and addiction. [Chou/p115/c2/1.1+1.3]

Because of the risks associated with opioids, HCPs should individualize treatment for every patient using non-opioid analgesics, opioids as needed and/or combination analgesics, and chronic opioid therapy in a progressive plan of pain management.

According to the World Health Organization: "If pain occurs, there should be prompt oral administration of drugs in the following order:

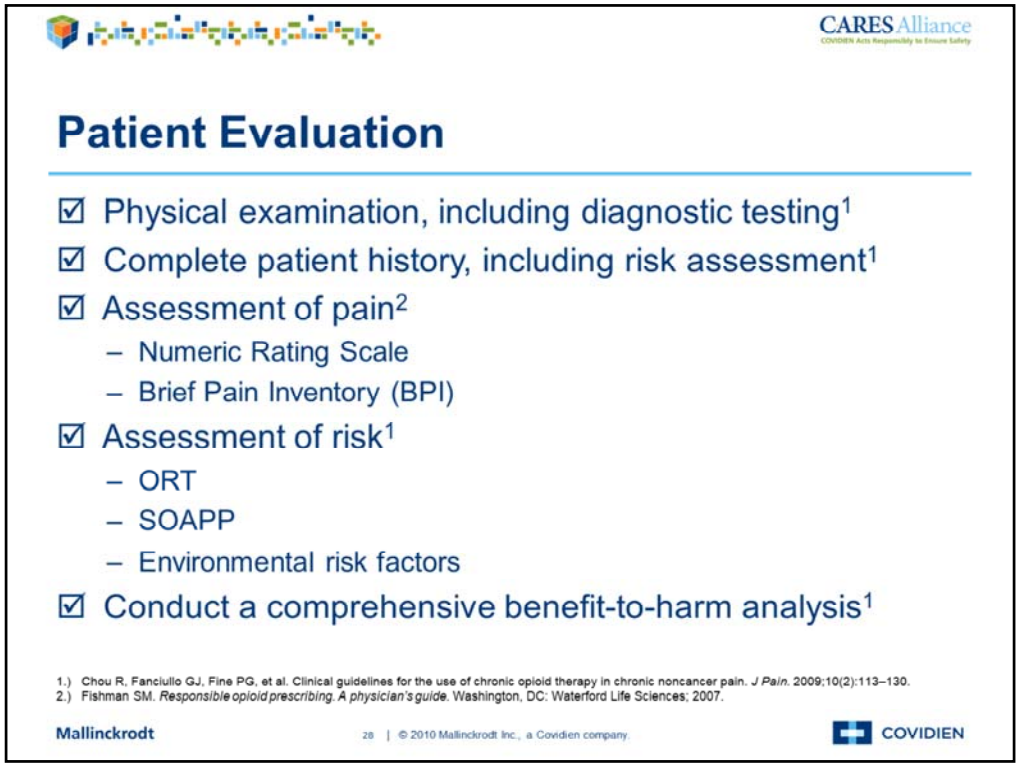
•Nonopioids (aspirin and paracetamol); then, as necessary,

•Mild opioids (codeine); then strong opioids such as morphine, until the patient is free of pain. To calm fears and anxiety, additional drugs – 'adjuvants' – should be used.

•To maintain freedom from pain, drugs should be given 'by the clock,' that is, every 3-6 hours, rather than 'on demand.'

This 3-step approach of administering the right drug in the right dose at the right time is inexpensive and 80%-90% effective. Surgical intervention on appropriate nerves may provide further pain relief if drugs are not wholly effective."
[http://www.who.int/cancer/palliative/painladder/en/]

HCPs may consider a trial of opioid therapy in a patient whose pain is moderate to severe, is having an adverse impact on function or quality of life, and in whom the potential therapeutic benefits outweigh the potential harms. [Chou/p115/c2/1.2]



To properly select a patient, an effective patient evaluation should be undertaken and include:

A comprehensive physical examination including appropriate diagnostic testing [Chou/p115/c2/1.3]

A thorough patient history including assessment of psychosocial factors and family history to aid in risk stratification [Chou/p116/c1/¶2]

A comprehensive benefit-to-harm analysis to determine the appropriateness of opioid therapy [Chou/p116/c1/¶2]

Appropriate diagnostic tests to assess the underlying pain condition and determine the suitability of treatment with nonopioid therapy [Chou/p116/c1/¶2]

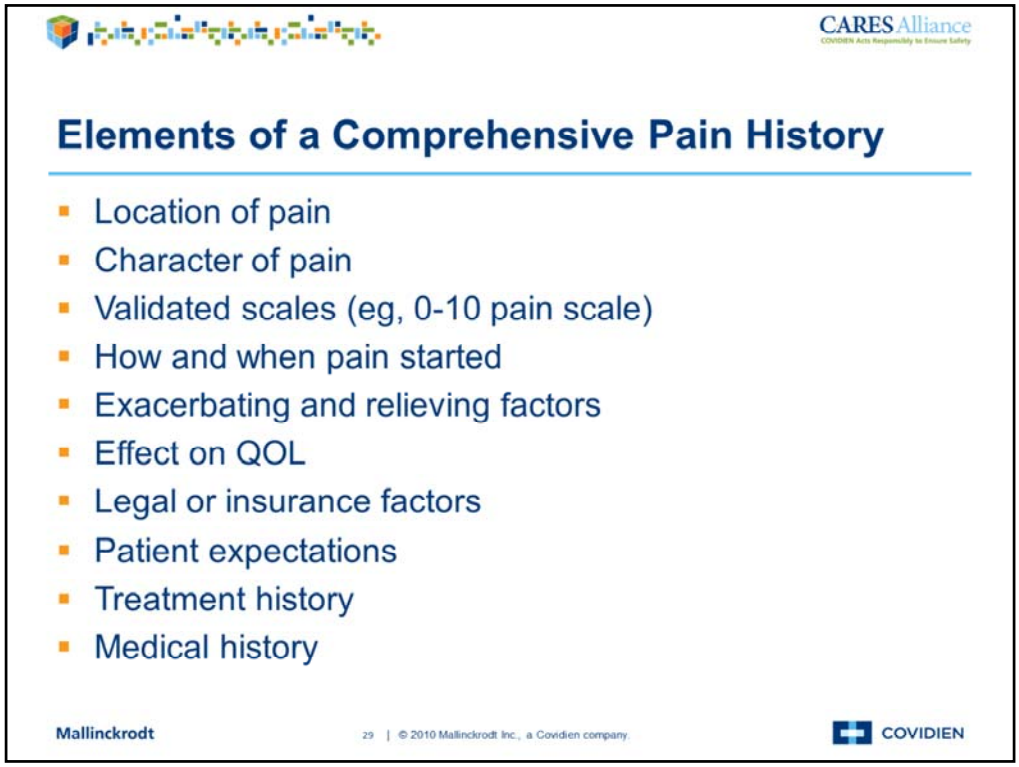
Characterization of the pain and assessment of its impact on the patient's ability to function and quality of life [Fishman/p19/¶3+Bullets–p20/Bullets]

- Numeric Rating Scale
- Brief Pain Inventory

Assessment of risk of abuse and addiction using patient and family history of substance abuse and validated risk assessment tools such as: [Chou/p116/c1/¶4;c2/¶2]

- Opioid Risk Tool (ORT)
- Screener and Opioid Assessment for Patients with Pain (SOAPP) v1.0 and the revised SOAPP (SOAPP-R)

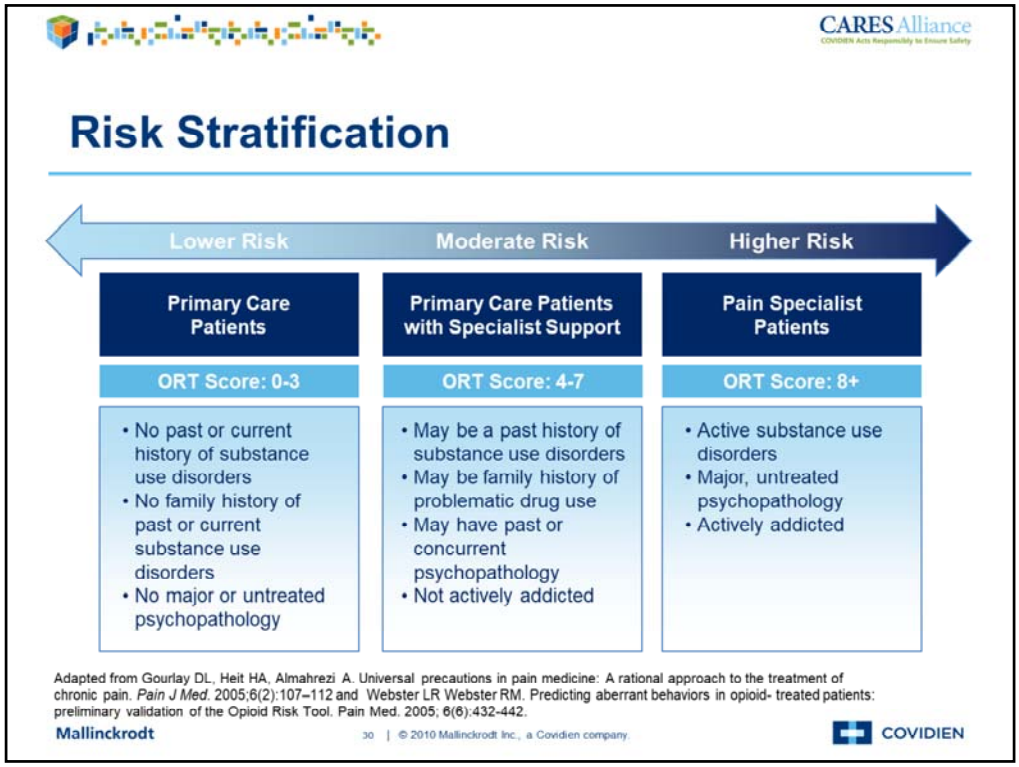
Conduct a comprehensive benefit-to-harm analysis to determine the appropriateness of opioid therapy [Chou/p116/c1/ ¶2]



A comprehensive pain history is an integral part of individualizing opioid therapy.

Elements of a comprehensive pain history include:

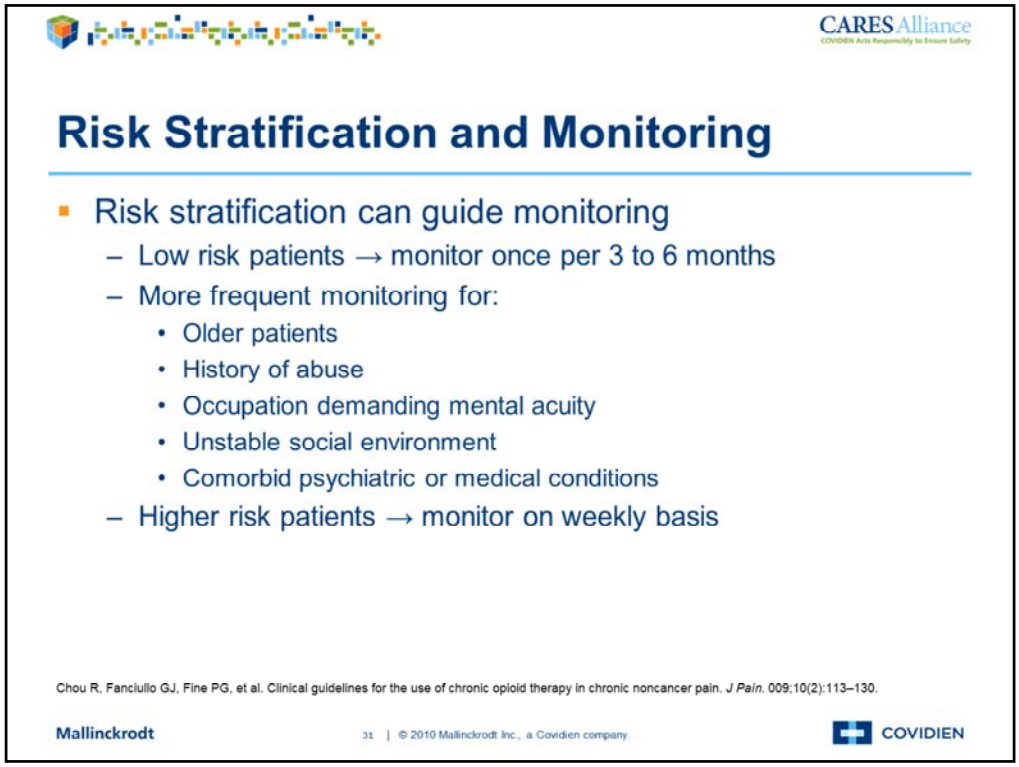
- The location of pain (ie, using body image on BPI)
- The character of the pain, such as continuous, intermittent, stinging, or shooting
- The normal, highest, and lowest pain intensity currently and in the past using the 0-10 scale
- Information on how and when the pain first started
- Information on the factors that make the pain better or worse
- Any involvement the patient has in legal or insurance processes
- The patient's expectation for treatment
- Any current or past treatment the patient received for pain
- Any underlying or coexisting diseases or conditions



Risk stratification is basing treatment on the tiers of a patient's risk factors. HCPs should then structure opioid therapy to accommodate the identified risk. [Chou/p115/c2/1.1]

Patients who are at lower risk and can be usually managed in a primary care setting are those with no past or current history of substance abuse disorder, no family history of past or current substance abuse disorder, and no major or untreated psychopathology.
Patients who are at moderate risk and can be managed in a primary care setting with support from a specialist are those that may have a past history of a treated substance abuse disorder, may have significant family history of problematic drug use, and may have a past or concurrent psychopathology yet are not actively addicted.
Patients who are at higher risk and can be managed by a pain specialist are those with active substance use disorder, major untreated psychopathology, or who are actively addicted.

This can be used as a practical framework to help determine which patients may be safely managed in the primary care setting, which should be comanaged with specialist support, and which should be referred on for management of their chronic pain condition in a specialist setting.



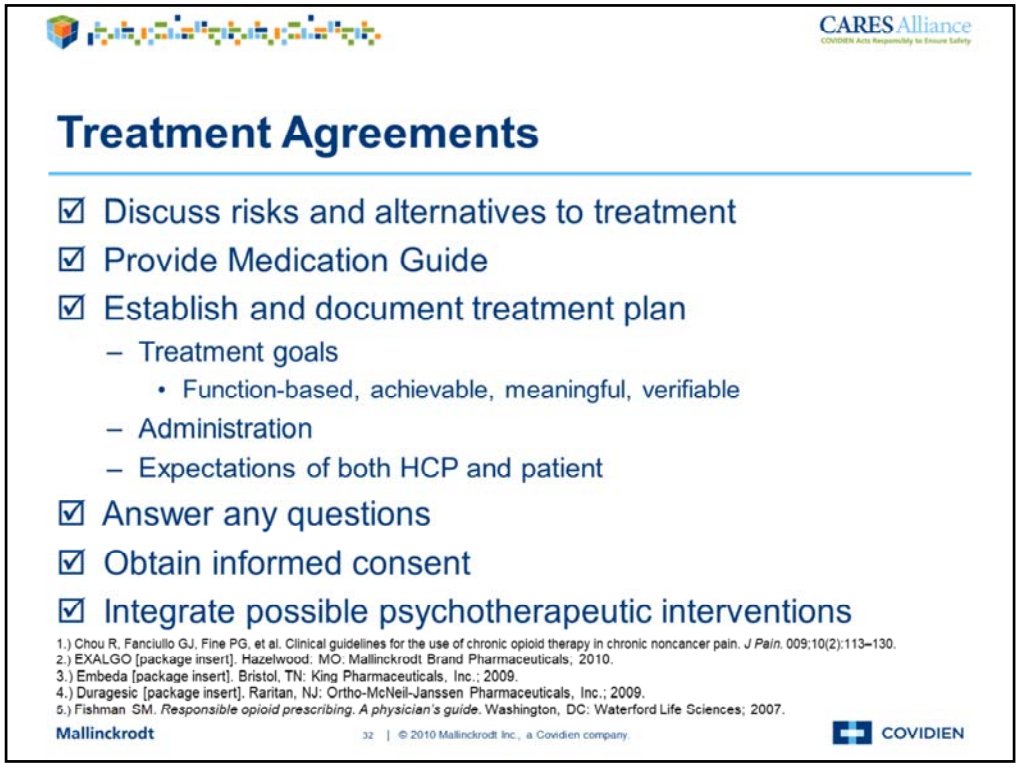
Risk stratification is also useful for guiding the HCPs' approach to monitoring:

In patients at low risk for adverse outcomes on stable doses of opioids, monitoring once every 3 to 6 months may be sufficient.

Patients who may need more frequent or intense monitoring include: older patients or those with a prior history of an addictive disorder, an occupation demanding mental acuity, an unstable or dysfunctional social environment, or comorbid psychiatric or medical conditions.

In patients at very high risk, monitoring on a weekly basis may be necessary. [Opioid Treatment Guidelines, 2009]

Monitoring can be done through diaries, written agreements, tablet counts, or lab tests. [Fishman 2007/p53/¶1; p55/Table]



The next step in mitigating risk is developing treatment agreements.

Before initiating treatment, HCPs should:

•Discuss the risks and alternatives to opioid analgesics [Chou/p117/c1/¶2]

•Inform patients about the risks and benefits associated with treatment and gain their consent before initiating a trial of opioid therapy [Chou/p116/c2/2.1] [FSMB/p4/¶2]

•For opioid analgesics with a Medication Guide, provide the Medication Guide to patients every time it is dispensed as it may contain important new information [EXALGO PI/p28/¶2] [Embeda PI/p10/c1/¶2] [Duragesic PI/p3/c2/¶8]

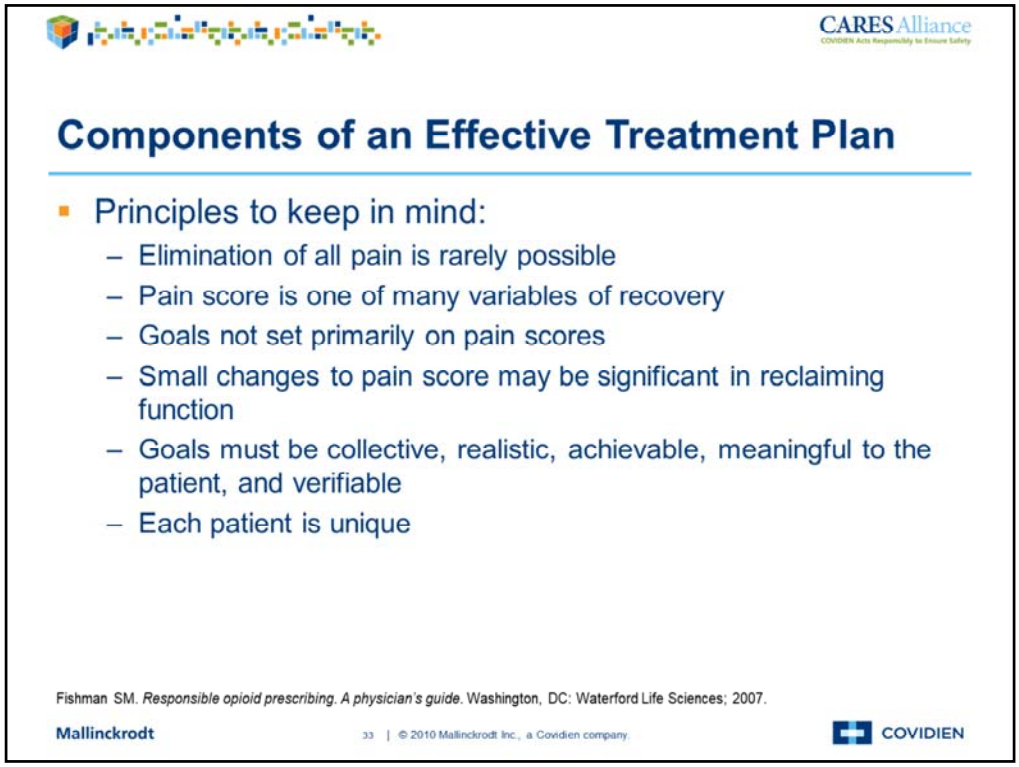
•Establish and document a treatment plan and an opioid use agreement, including: goals of therapy, how opioids will be prescribed and taken, and expectations for follow-up and monitoring; [Chou/p116/c2/2.1] [FSMB/p3/¶2] [Fishman/p45/¶2] treatment goals should be function-based, achievable, meaningful to the patient, and verifiable

•Psychotherapeutic interventions, including cognitive-behavioral therapy, should routinely be integrated into the pain management plan [Chou/p121/c2/9.1+¶4]

The treatment agreement can enhance the patient-HCP relationship and provides an opportunity for patient education and counseling. Treatment agreements can engage patients by making them active participants in their care, clarifying roles, motivating adherence, avoiding misunderstandings, and establishing a foundation for future decision making. [Fishman/p47/¶2+Bullets]

Document the treatment plan, including patient and HCP responsibilities and expectations for the appropriate and safe use of opioids, in an opioid use agreement. [Chou/p117/c1/¶3]

The HCP should make sure that all patient questions have been answered.



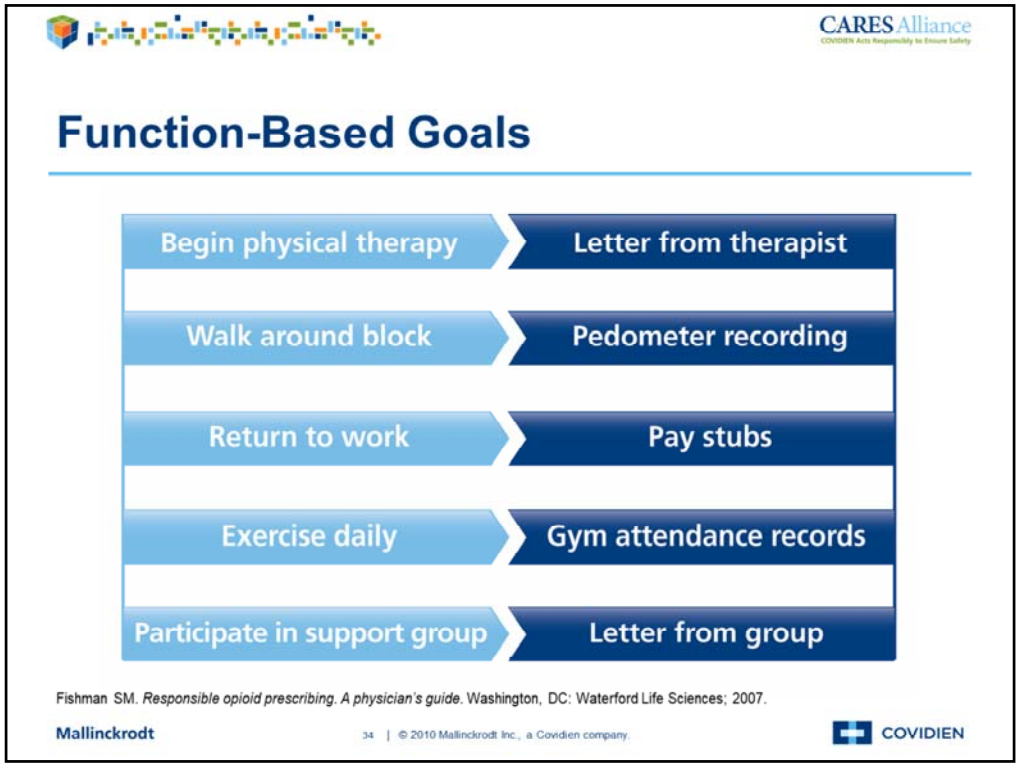
Because it is difficult to completely relieve pain, physicians may consider shifting from focusing on analgesia to focusing on functioning (eg, get out of bed, go back to work part time, attend more events outside the home) when developing treatment plans.

Traditional pain scales can imply that “zero” pain is attainable. Function-based therapy can increase a patient’s QOL and reduce their burden of pain. [Fishman 2007]

Sometimes a small change in pain intensity can translate into a very significant improvement in QOL. [Fishman 2007]

Function-based treatment goals should be collaborative, realistic, achievable, meaningful to the patient, and verifiable. [Fishman, 2007]

Examples of verifiable functional goals include pay stubs (if the goal was to return to work) or gym attendance records (if the goal was to start exercising). [Fishman 2007/p55/Table]



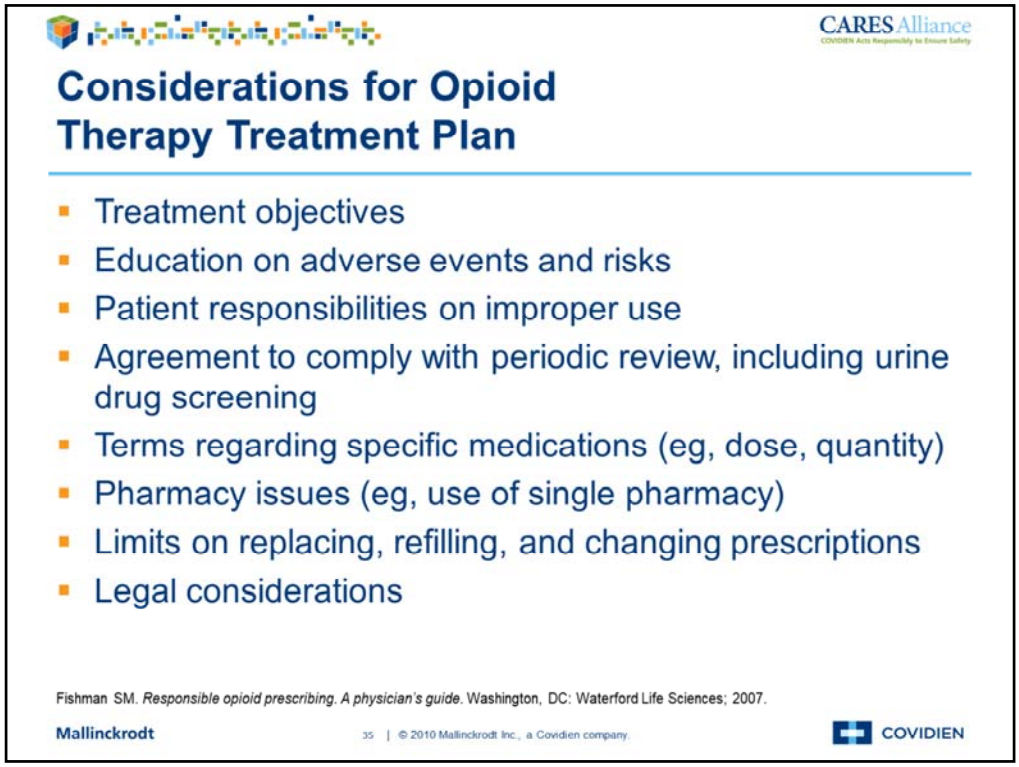
Periodic review refers to follow-up after initiating a treatment plan.

When validation requires a report from family or friend, attempt to have person come in with patient.

No validation scheme is 100% foolproof – repeated request for verification quickens discovery of dysfunction or deception.

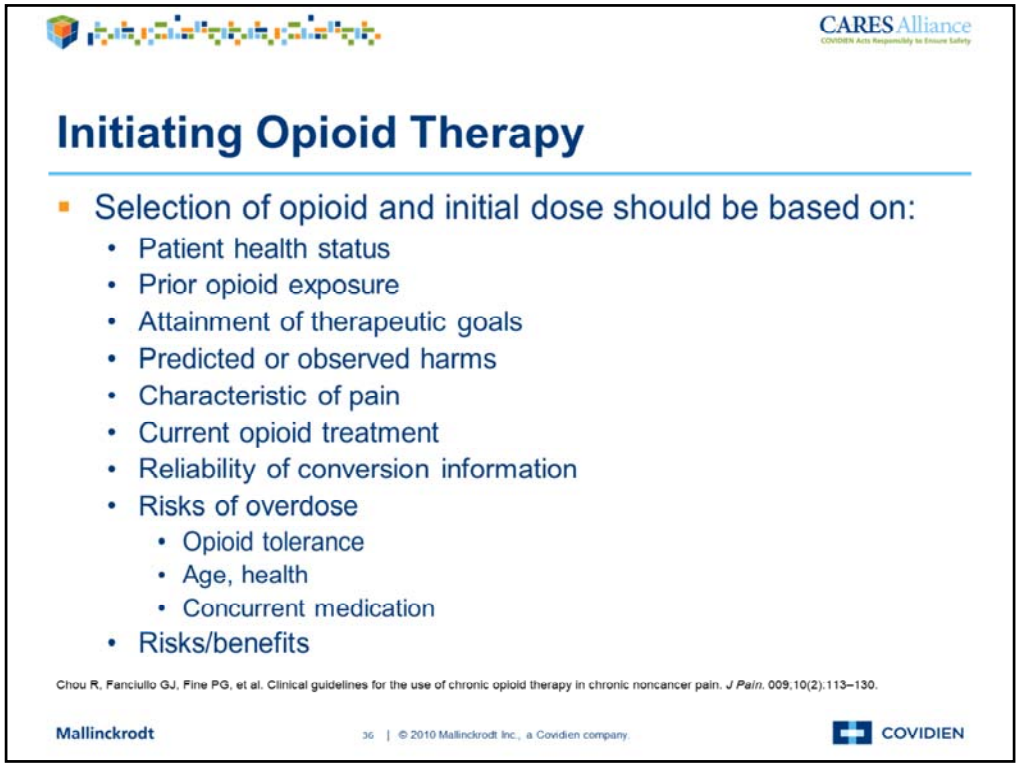
The point of verification is to motivate the patient and provide the physician with information and documentation if treatment is not working.

Finding the right level for a goal – higher or lower – can be done through the review process.



Considerations for an opioid therapy treatment plan or agreement include:

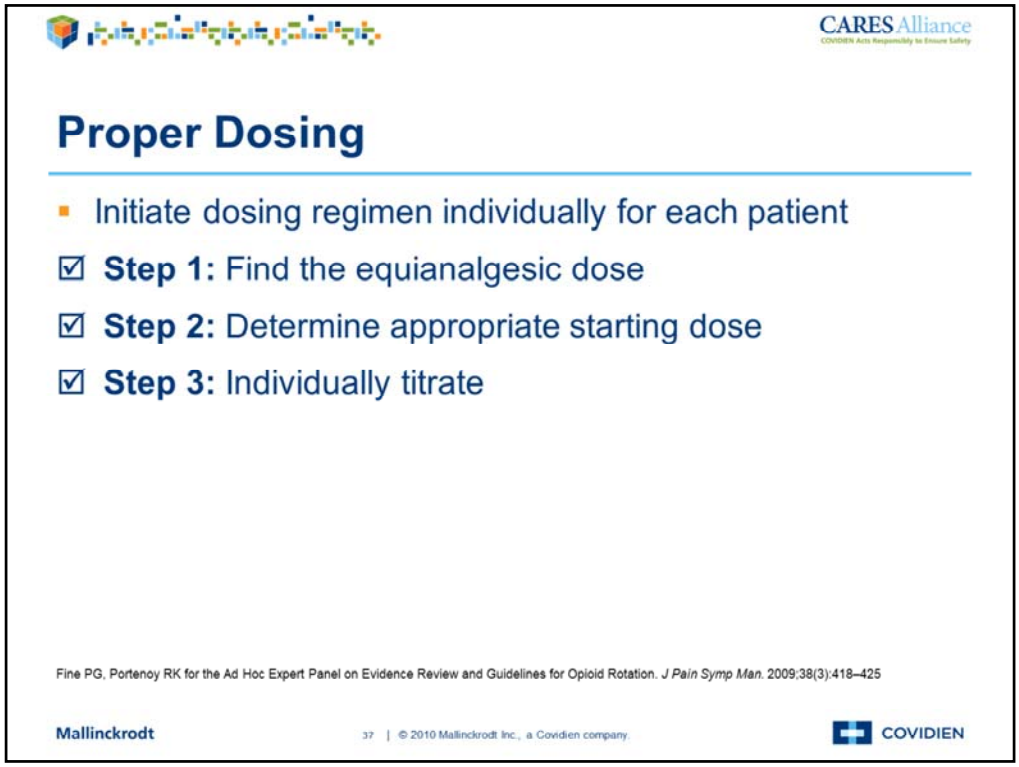
- Treatment objectives
- Education on adverse events and risks
  - Drug risks can include drug interactions, masking conditions, pregnancy
- Patient responsibilities on improper use
  - Improper use includes overdosing, seeking medication elsewhere, selling medication, stopping medication abruptly
- Agreement to comply with periodic review, including UDS
- Terms regarding specific medications (eg, dose, quantity)
  - Specific medications include long-acting, generic, brands, strength, and quantity
- Pharmacy issues (eg, use of single pharmacy)
- Limits on replacing, refilling, and changing prescriptions
- Limits on refills include phone allowances, mailing or faxing policy, normal office hours
- Legal considerations



Following the development of a treatment plan, initiation of opioid therapy should be viewed as a short-term trial of several weeks' to several months' duration to determine appropriateness. [Chou/p117/c1/3.1–c2/3.2+¶1]

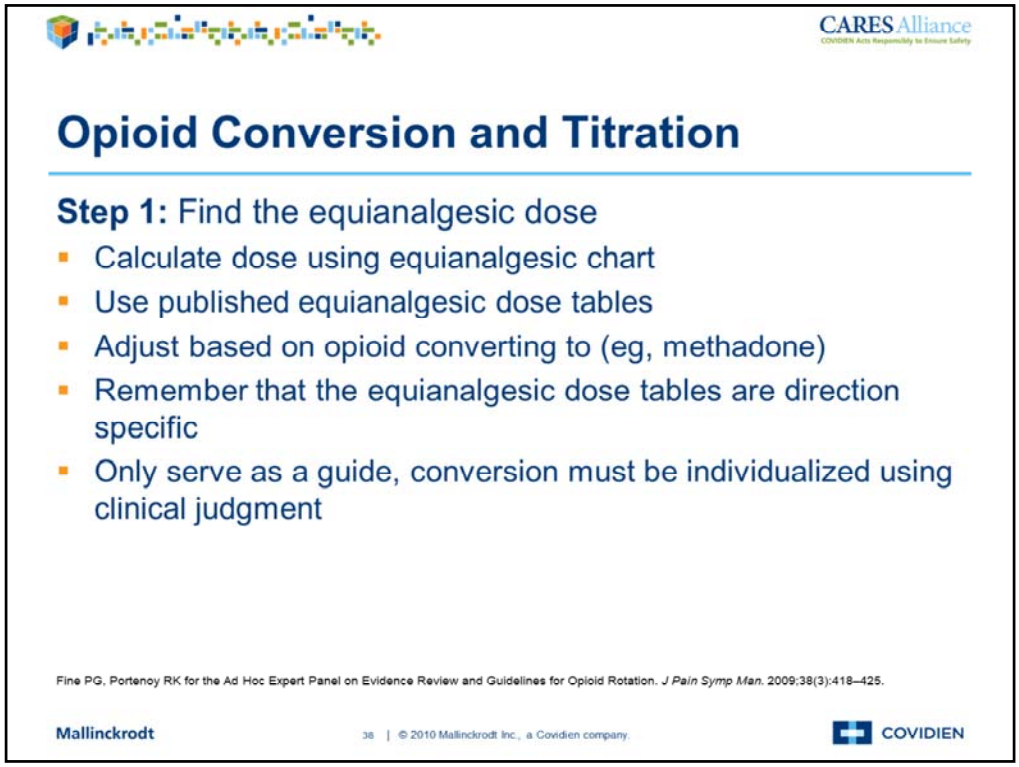
Selection of the opioid to be prescribed, initial dosing, and titration should be individualized based on each patient's: [Chou/p117/c2/3.2]

- Health status
- Prior opioid exposure
- Attainment of therapeutic goals
- Predicted or observed harms
- Type and severity of the patient's pain
- Daily dose, potency, and specific characteristics of the opioid the patient has been taking previously
- Reliability of the relative potency estimate used to calculate the equivalent opioid dose needed
- Risk factors for overdose, including:
    - The patient's degree of opioid tolerance
    - The patient's age, general condition, and medical status
    - Concurrent use of nonopioid analgesics and other medications, such as those with CNS activity
- Risk factors for misuse, abuse, addiction, or diversion, including a prior history of abuse, addiction, or diversion
- Balance between the risks and benefits of opioid therapy



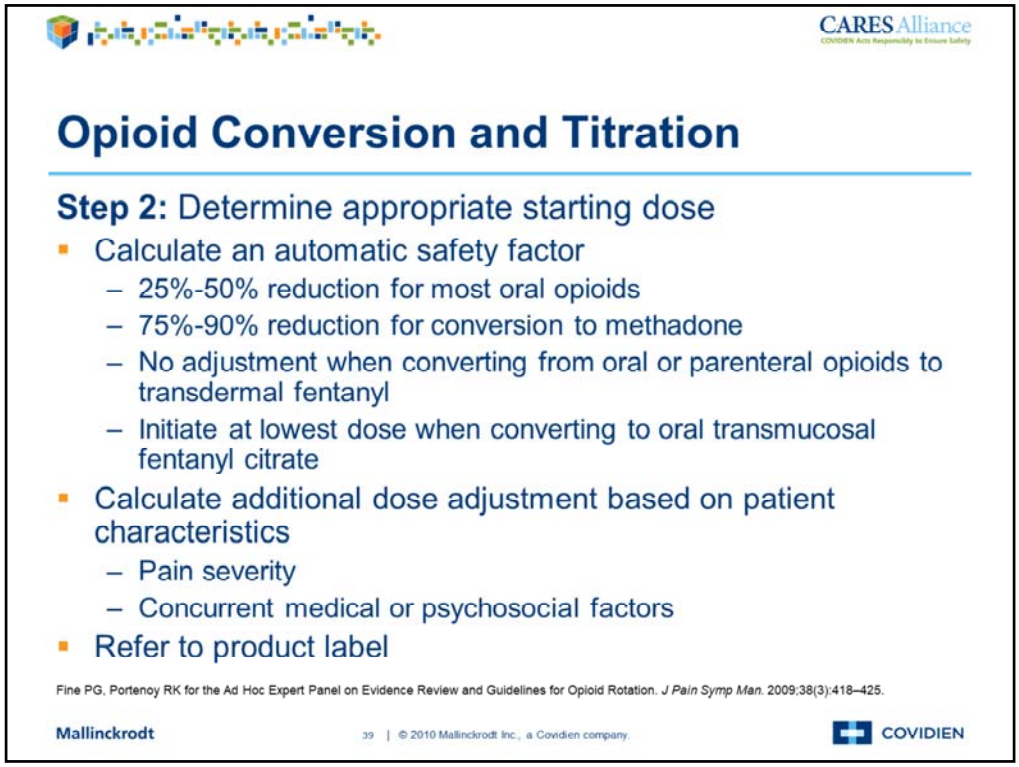
Proper opioid dosing begins with three steps: Step 1 involves utilization of existing equianalgesic dose tables for conversion from existing opioid therapy; Step 2 requires an automatic and then individualized adjustment to the calculated starting dose based on individual clinical risk assessment in order to reduce the risk of unintentional overdose; and Step 3 involves individual titration to adequate pain relief with tolerable side effects no more frequently than every 3 to 4 days.

Step 1
First, sum the total daily dose of current opioid therapy, then multiply by the conversion ratio to calculate the approximate total daily dose of new medication.
Step 2
To determine the approximate starting dose, first calculate the automatic dose adjustment and then calculate an additional dose adjustment considering individual clinical risk assessments including pain severity and medical or psychosocial characteristics.
Step 3
Involves individual titration to adequate pain relief with tolerable side effects no more frequently than every 3 to 4 days. Health care professionals should assess pain relief and adverse reactions frequently.



When initiating treatment, opioid conversion may be necessary if patient is already taking opioid medication. A recent Ad Hoc Expert Panel on Evidence Review and Guidelines for Opioid Rotation recommends utilization of existing equianalgesic dose tables when converting patients from existing opioid therapy. [Fine/p422/c1/¶1+2]

These equianalgesic dose tables are found in the prescribing information for each product. Because of several limitations of these conversion ratios, the Panel also recommended additional dose adjustments after calculation of the equianalgesic dose to determine the approximate starting dose.



To reduce the risk of unintended overdose, adjust the calculated conversion ratio based on a clinical assessment of risk.

•Calculate an automatic safety factor

•25%–50% reduction in the equianalgesic dose for most oral opioids

•75%–90% reduction in the equianalgesic dose for patients switching to methadone

•Adjustment not required when converting from oral or parenteral opioids to transdermal fentanyl

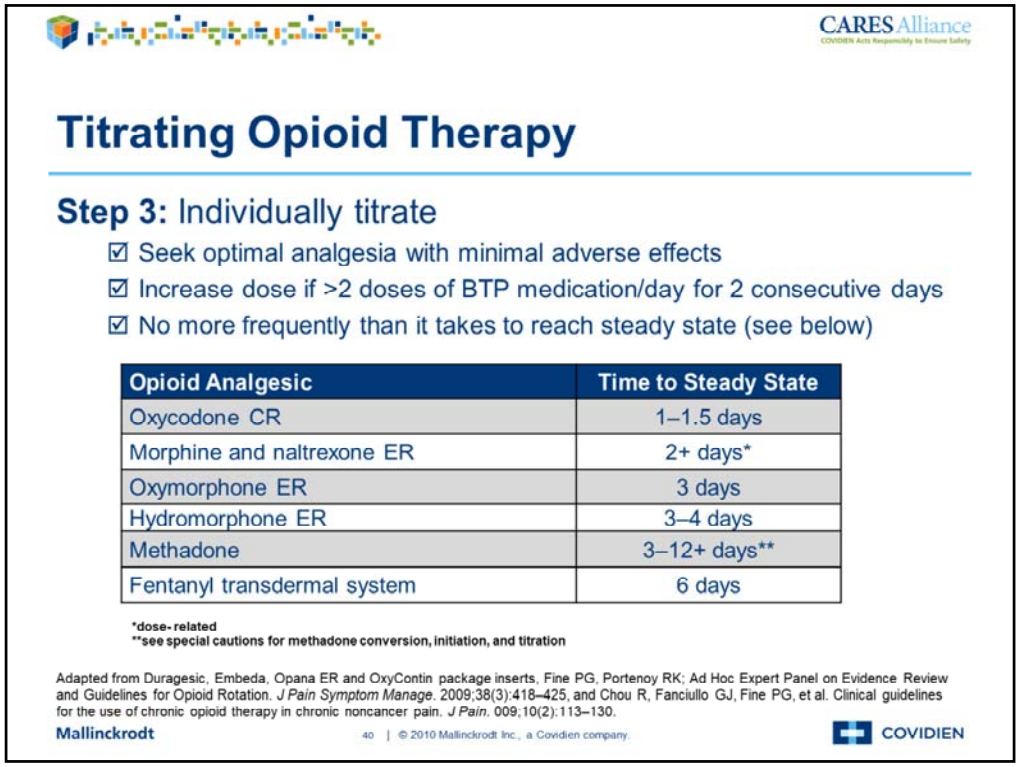
•Initiate at the lowest available dose regardless of previous opioid regimen when converting to oral transmucosal fentanyl citrate

Calculate an additional dose adjustment based on assessment of patient characteristics, including:

•Pain severity at the time of conversion

•Existence of other medical or psychosocial factors that potentially alter potency or the likelihood that the initial dose will be analgesic, relatively free of adverse effects, and unlikely to precipitate withdrawal

HCPs should refer to the product labeling for additional information concerning risks and safe use.



When initiating treatment, it is important to titrate each patient individually for optimal analgesia with minimal adverse effects.

HCPs should have a strategy to frequently assess the patient's initial response to opioid treatment and titrate to optimize outcomes [Fine/p422/Table 1]—that is, to the dose that provides adequate pain relief with tolerable adverse events.

Titration should take into account the time required for the new opioid to reach steady state, which may range from 24–36 hours to 6 days. [EXALGO PI/p6/Bullet 4] [Embeda PI/p2/c2/Bullet 1] [Opana PI/p3/¶8] [Oxycontin PI/p5/¶2] [Duragesic PI/p6/c2/¶6] [Methadose PI/p11/¶6]

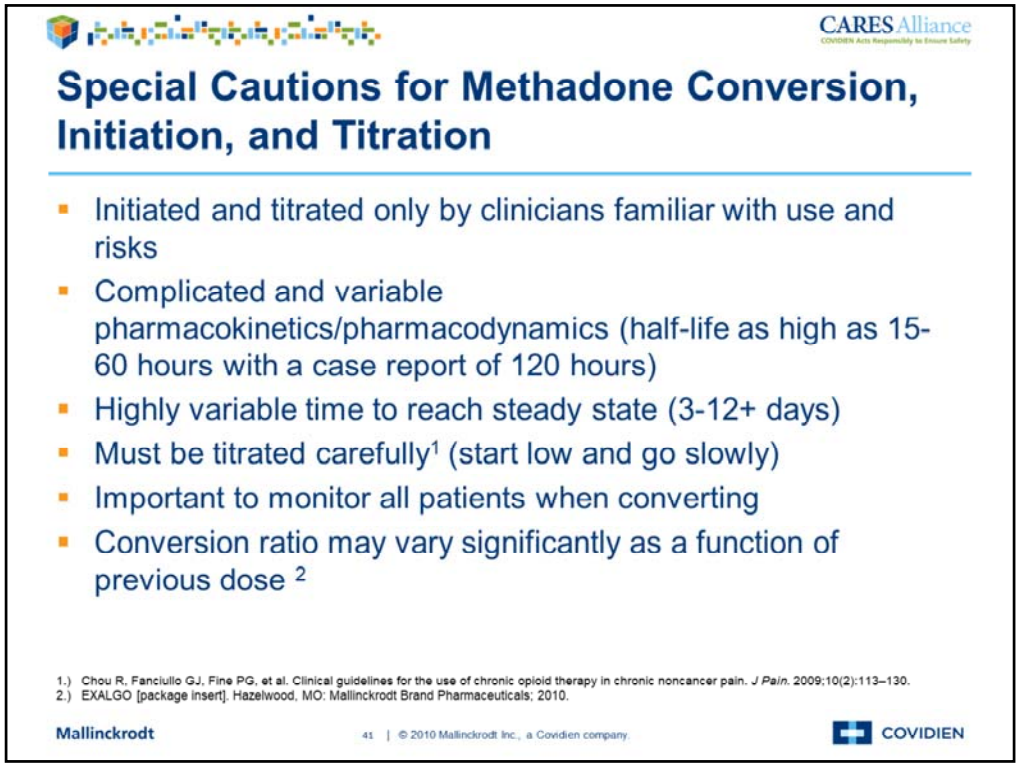
Titrate no more frequently than it takes to reach steady state and increase dose if greater than 2 BTP medication doses are taken per day for 2 consecutive days.

Time to steady state of selected long-acting opioids:

OxyContin CR	1-1.5 days
Morphine and naltrexone ER	2+ days*
Oxymorphone ER	3 days
Hydromorphone ER	3-4 days
Methadone	3-12+ days**
Transdermal fentanyl system	6 days

*dose-related

**see special cautions for methadone conversion, initiation and titration

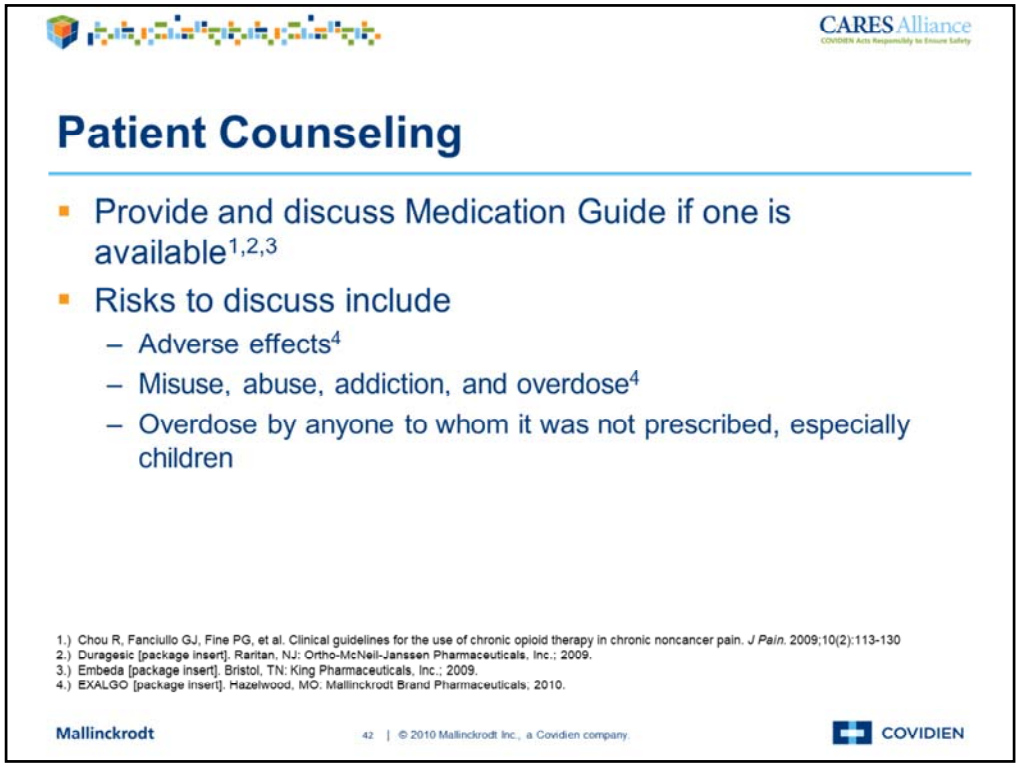


Methadone should be initiated and titrated cautiously, by clinicians familiar with its use and risks. It is characterized by complicated and variable pharmacokinetics and pharmacodynamics. [Chou/p117/c2/4.1–p118/c1]

Due to its very long and variable half-life, methadone must be titrated carefully to avoid the potential for delayed adverse events such as overdose. [Chou/p118/c1¶2]

It is therefore extremely important to monitor all patients closely when converting from methadone to other opioid agonists. [EXALGO PI/p6/Bullet 1]

The ratio between methadone and other opioid agonists may vary widely as a function of previous dose exposure. [EXALGO PI/p6/Bullet 1]



Before initiating treatment with opioid analgesics, counsel patients and caregivers on opioid risks and safe use and handling.[1, 3, 4] Instruct patients to read the Medication Guide each time their opioid analgesic is dispensed because new information may be available.[2, 3, 4]

Topics to discuss with patients before initiating opioid therapy include:

•Risk

•Safe use

•Safe handling

Risks to discuss include:

•Potential for common opioid-related adverse effects, such as constipation, nausea, and sedation[1]

•Potential for serious risks, including misuse, abuse, addiction, and overdose[1]

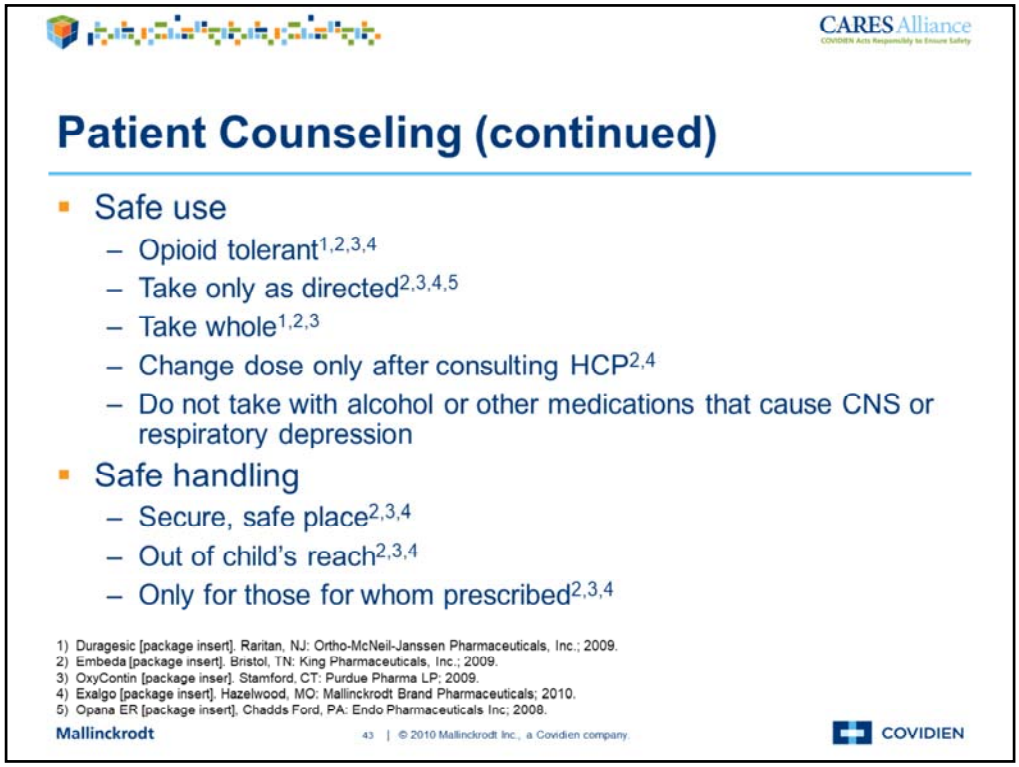
•Potential risk of fatal overdose to anyone for whom it was not prescribed (especially children)

1)Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009;10(2):113-130.

2)Duragesic [package insert]. Raritan, NJ: Ortho-McNeil-Janssen Pharmaceuticals, Inc.; 2009.

3)Embeda [package insert]. Bristol, TN: King Pharmaceuticals, Inc.; 2009

4)Exalgo [package insert]. Hazelwood, MO: Mallinckrodt Brand Pharmaceuticals; 2010.



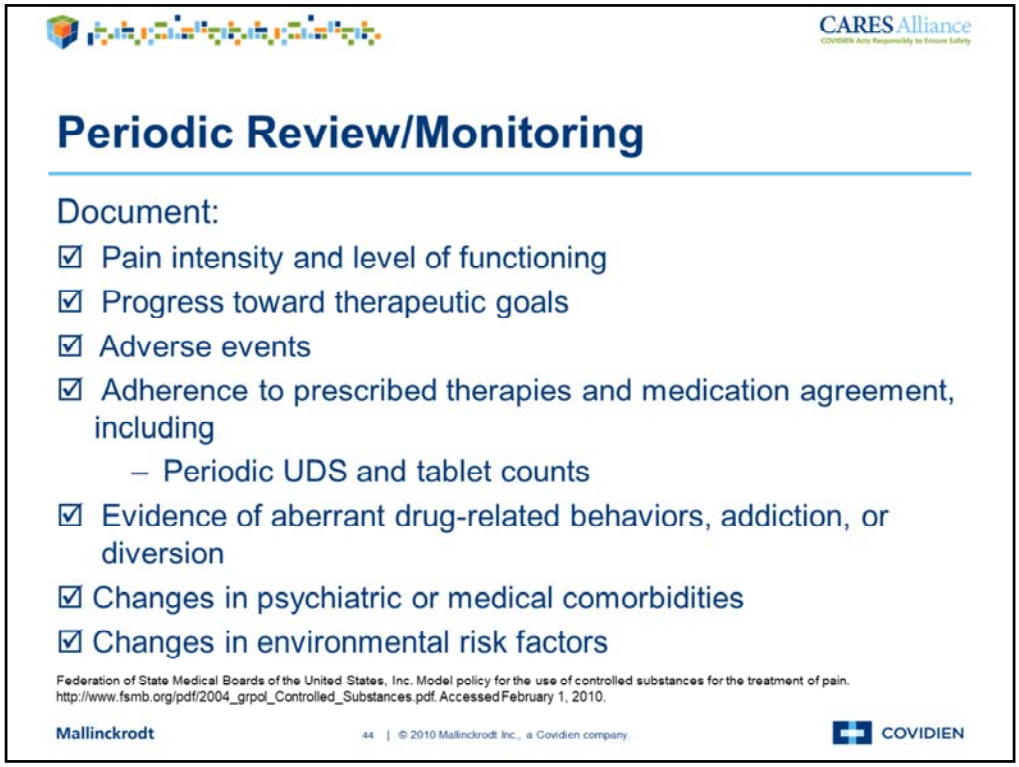
Safe Use

- Certain opioids and high doses of most opioids are only for patients who are already receiving opioid pain medicine and whose bodies are used to taking these medications[1, 2, 3, 4]
- Opioid analgesics must be taken only as directed[2, 3, 4]
- Oral tablets designed to be swallowed whole should never be broken, chewed, dissolved, or crushed; the ingredients should not be snorted, injected, or inhaled; and transdermal opioids should not be taken orally, as doing so may result in a fatal overdose[1, 2, 3, 4, 5]
- The opioid dose should not be changed without first consulting an HCP[2, 4]
- Opioids should not be taken with alcohol or other medications that cause CNS or respiratory depression

Safe Handling

- Opioid analgesics should be kept in a secure place out of the reach of anyone for whom they are not prescribed, especially children[2, 3, 4]
- Opioid analgesics should only be taken by the individuals for whom and for the conditions for which they have been prescribed[2, 3, 4]
- Opioid analgesics are subject to misuse, abuse, addiction, overdose, and diversion, and should therefore be carefully stored to prevent theft[2, 3]
- It is against the law to sell or give away opioid medication[3]
- HCPs should counsel women of childbearing potential about the risks and benefits of chronic opioid therapy during pregnancy and after delivery, and should encourage no use of chronic opioids during pregnancy unless the potential benefits outweigh risks[5]
- HCPs should counsel patients receiving chronic opioid therapy about transient or lasting cognitive impairment that may affect driving and work safety[5]

1) Duragesic [package insert]. Raritan, NJ: Ortho-McNeil-Janssen Pharmaceuticals, Inc.; 2009.
2) Embeda [package insert]. Bristol, TN: King Pharmaceuticals, Inc.; 2009.
3) OxyContin [package inser]. Stamford, CT: Purdue Pharma LP; 2009
4) Exalgo [package insert]. Hazelwood, MO: Mallinckrodt Brand Pharmaceuticals; 2010.
5) Opana ER [package insert], Chadds Ford, PA: Endo Pharmaceuticals Inc; 2008.



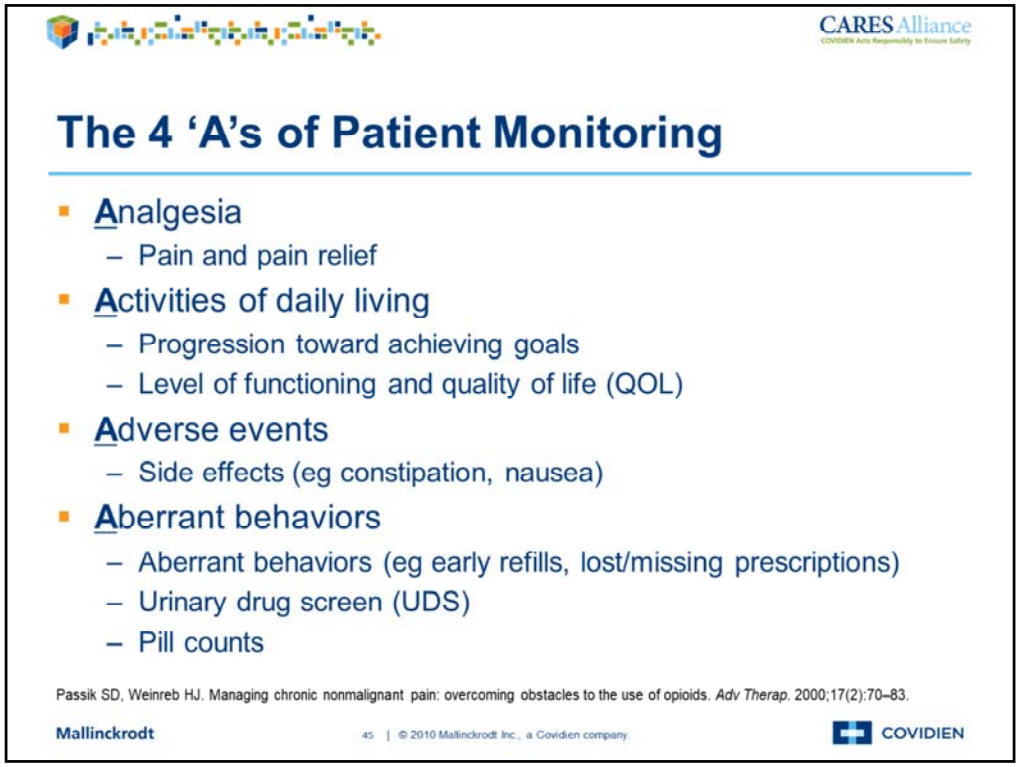
After initiating chronic opioid therapy, assessment is another important tool to mitigate risk. Patients should be periodically re-evaluated to confirm the continued need for around-the-clock opioid therapy, as well as the appropriateness of current therapy based on pain control and adverse events. [EXALGO PI/p7/2.2] [Embeda PI/p2/c2/2.4] [Opana PI/p21/¶6] [Oxycontin PI/p25/¶4] [Duragesic PI/p5/c1/¶8]

HCPs should periodically review the course of the patient's treatment for pain as well as any new information that may become available about the etiology of the patient's pain or their state of health. [FSMB/p4/¶3]

Patients should also continue to be monitored for clinical risk of opioid abuse, addiction, or diversion, particularly with high-dose formulations. [EXALGO PI/p7/2.2]

Periodic reviews, like opioid treatment itself, should be individualized for each patient and guided by the HCPs' own judgment. [Fishman/p53/¶2]

Satisfactory responses warranting continued opioid therapy include decreased pain, increased ability to function, and improved quality of life. [FSMB/p4/¶3] Objective evidence of improvement can be obtained directly from the patient as well as from family members and caregivers. [FSMB/p4/¶3] Family members and caregivers may be asked to accompany the patient on follow-up visits. [Fishman/p55/¶2]



Based on the CDC's "Universal Precautions" that were aimed at reducing the risk of transmitting infectious disease:

Similar to CDC's precautions in that incorrect treatment can harm both the patient (health) and the physician (liability).

"Universal Precautions" help to ensure that a patient's quality of life is optimized.

Four A's are goals to optimize:

Analgesia, avoid Adverse drug events, Activities of daily life, and avoid Aberrant medication-related behaviors.

Clinicians should routinely carry out a thorough clinical assessment for presence of aberrant drug-related behaviors, substance use, and psychological issues. One tool to aid in monitoring patients during the course of opioid therapy is the 4As of outcome assessment: [Passik/p78/¶1+2;p79/¶1+2]

Analgesia (sustained efficacy): Pain must be monitored and documented during treatment with opioid analgesics and should be recorded at baseline and at all subsequent office visits using a validated scale for rating pain intensity. [Passik/p78/¶1]

Activities of daily living (functional status): Progress toward achieving therapeutic goals, including improvement in activities of daily living and psychosocial functioning, is necessary to show benefit of opioid therapy and should be documented at each office visit. [Passik/p78/¶2]

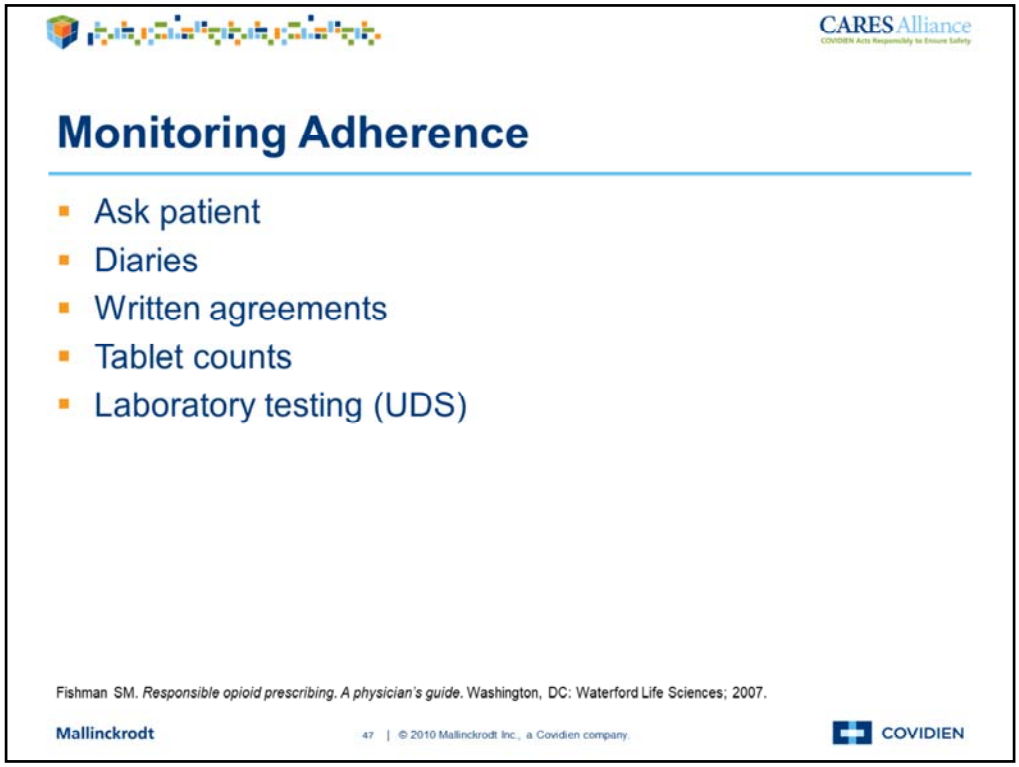
Adverse effects: Optimal pain relief with minimal side effects is the goal of pain management, and HCPs should monitor and manage opioid-associated adverse effects throughout treatment. [Passik/p79/¶1]

Aberrant behaviors: Aberrant behaviors indicative of misuse, abuse, and addiction may arise in patients receiving long-term opioid therapy, and should therefore be assessed at every office visit and addressed if present. [Passik/p79/¶2]

Affect: Due to the relationship between potential aberrant drug-related behaviors and comorbid mood abnormalities such as anxiety and stress, clinicians may consider periodically evaluating "affect" as a fifth "A."

When assessing the fourth A, Aberrant behavior, behaviors suggestive of addiction include: [AAPM-APS-ASAM/p2/¶4]

- Inability to take medications on schedule
- Taking multiple doses at once
- Frequent reports of lost or stolen prescriptions
- Doctor shopping
- Isolation from family and friends
- Concomitant use of non-prescribed psychoactive drugs
- Use of analgesic medications for non-analgesic effects
- Nonadherence to other treatments or evaluations
- Insistence on rapid-onset formulations or routes of administration
- Reports of no pain relief whatsoever with non-opioid analgesics



Treatment cannot work if the patient does not adhere to it.

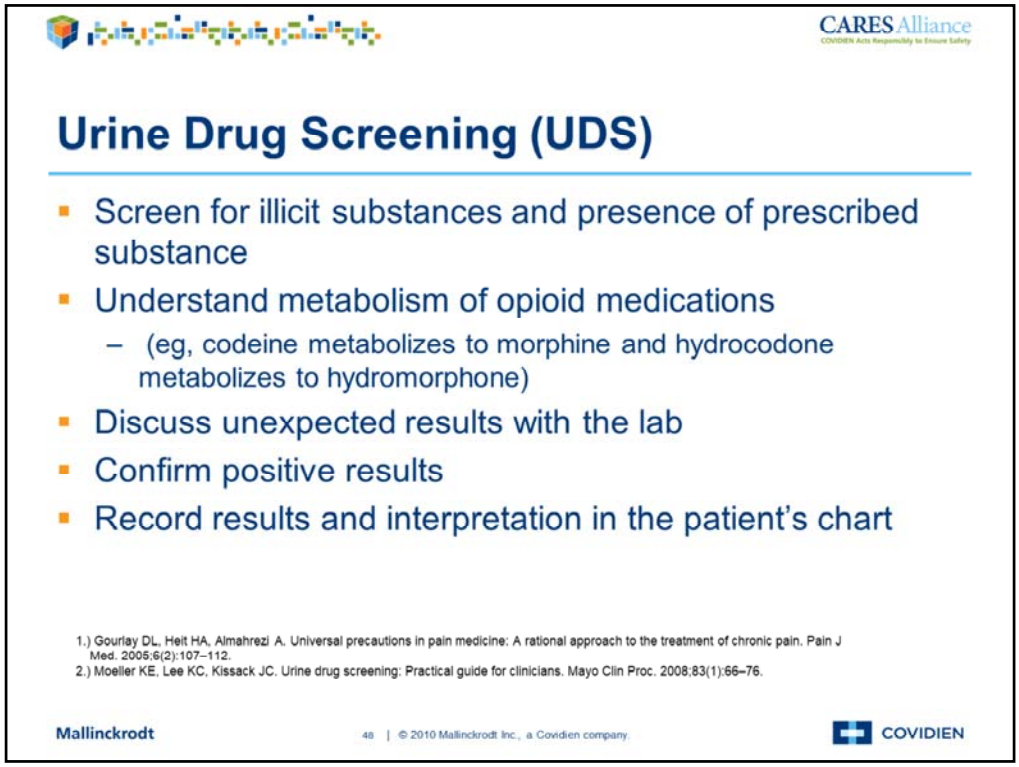
Asking the patient is the easiest; effective monitoring usually involves several techniques.

Tablet counts can be unreliable. Diaries can be subjective and interviews can be subject to favorable recall bias.

Laboratory testing is popular but can be compromised by custody of specimen, lab methodologies, and lab interpretation.

Urine is often used in testing because of ease of acquisition, simple testing methods, and longer duration of positive test results. However, urine is seldom quantitative.

Serum offers quantitative data but is rarely justified.



Urine medication screening forms part of the universal precautionary approach to managing the risk of opioid abuse. A urine sample is taken and can be used to monitor the presence of drug classes or specific drugs. The results of the urine drug test should be recorded on the patient's medical chart.

Urine screening is a standard routine drug surveillance method. However, its validity can be compromised. Results are also dependent on sample pH and volume; patient body weight and metabolism; the specific medications and their pharmacokinetics; the amount, dosage interval, and route of administration; and treatment duration. As such, it is very important to communicate with the laboratory at all stages in the screening process.

The window of detection for urine screening ranges from around 12 to 72 hours. It is also worth asking about the thresholds for positive and negative results. Another factor is the sensitivity and specificity of the tests.

Discuss any unexpected results with the lab. Positive results should be confirmed by a second test.

Screening should be considered a collaboration with the patient rather than a way to catch them or prove that they have been "cheating."

UDS results

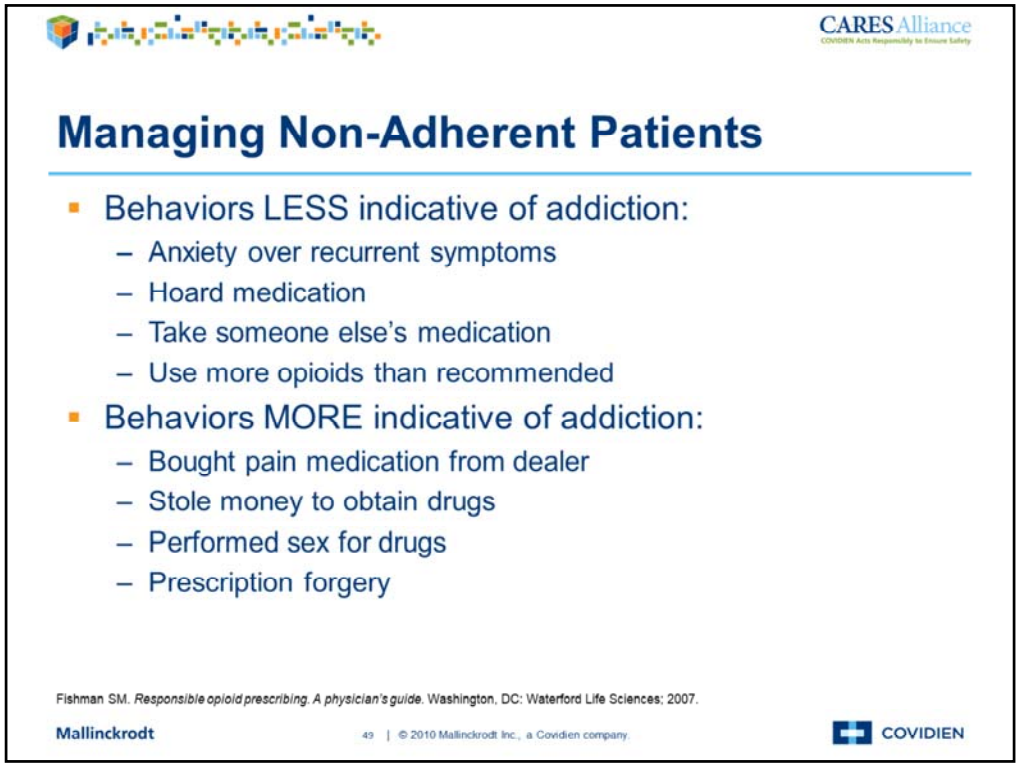
– Consult with laboratory regarding ANY unexpected results

– False positives: Note that codeine is metabolized into morphine, and hydrocodone into hydromorphone. Thus, do not be alarmed if morphine or hydromorphone are found in the urine of patients you are treating with codeine or hydrocodone. There are other causes of "false positives" as well

– Schedule an appointment to discuss abnormal/unexpected results with the patient; discuss in a positive, supportive fashion to enhance readiness to motivational enhancement therapy (MET) opportunities

– Use results to strengthen the healthcare professional-patient relationship and to support positive behavior change

– Chart results and interpretation



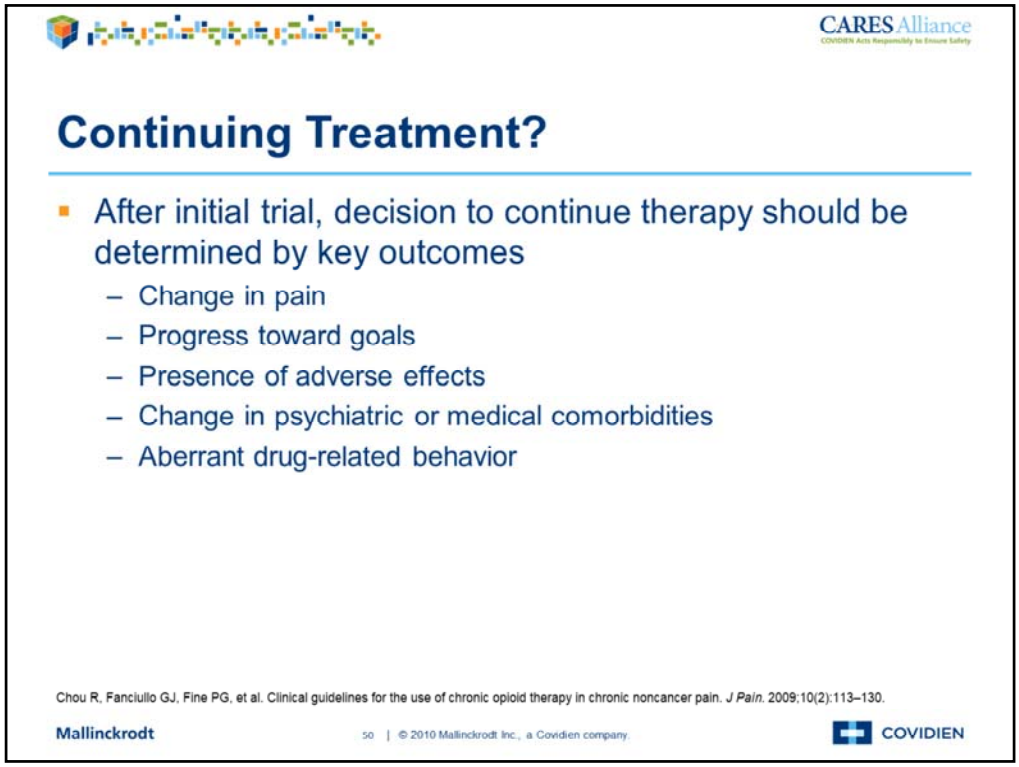
Non-adherence is not necessarily indicative of addiction.

Suspicion of non-adherence should prompt a thorough investigation, not a summary judgment.

Pseudoaddiction: Patients who are receiving an inadequate dose of opioid medications and seek more.

Other behaviors less indicative of addiction: Drinking or smoking to relieve pain, expressing worry over changing to a new drug, asking for second opinion about medication, using opioids to treat other symptoms.

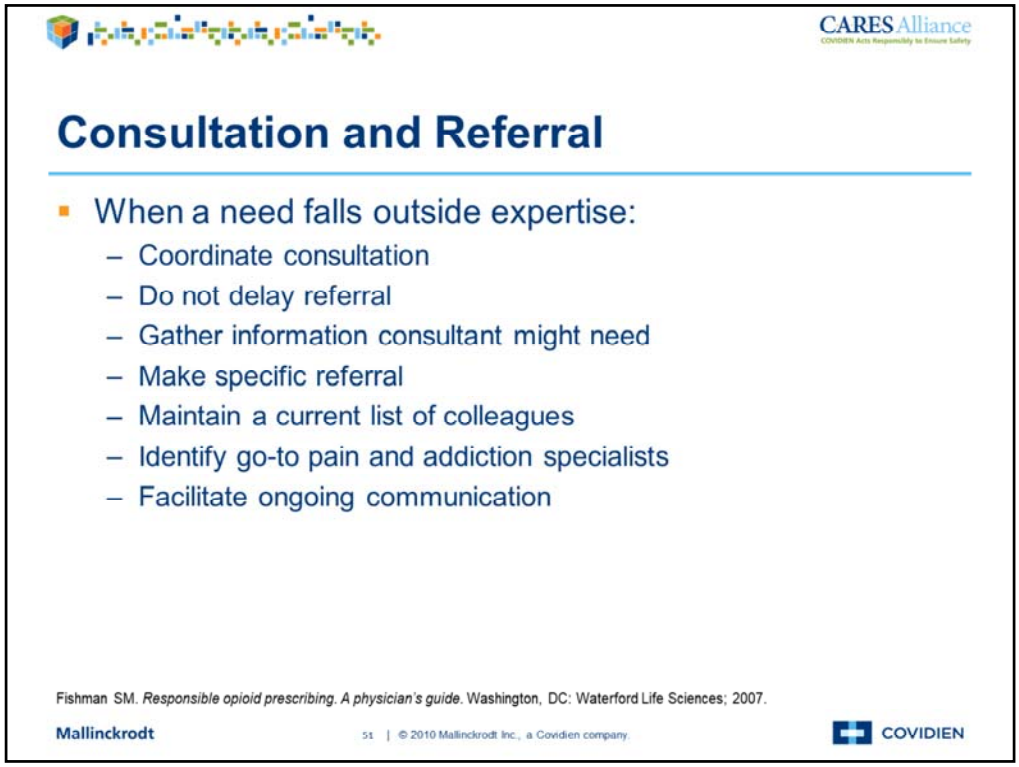
Other behaviors more indicative of addiction: Seeing 2 doctors at once without them knowing, stealing drugs from others, selling prescription drugs.



Assessment and monitoring may uncover issues with treatment and discontinuation of therapy may be considered. The decision to continue opioid therapy after the initial trial should be based on several key outcomes: [Chou/p117/c2/¶1]

- Progress in meeting defined therapeutic goals
- Presence of adverse effects
- Change in underlying pain condition
- Change in psychiatric or medical comorbidities
- Identification of aberrant drug-related behavior, addiction, or diversion

HCPs should evaluate patients engaging in aberrant drug-related behaviors for appropriateness of opioid therapy or need for restructuring of therapy, referral for assistance in management, or discontinuation of opioid therapy. [Chou/p119/c1/6.2]



Because patients which chronic noncancer pain have more comorbidities and are in greater need of health care services than other patients, referrals and consultation are often a necessary aspect of continuing opioid treatment. [Chou/p122/c2/¶1]

When such circumstances arise, HCPs should refer patients to clinicians who possess the specialized skills required and coordinate patient consultation with, and facilitate communication between, these other health care professionals as needed. [Fishman/p67/¶3–p68/¶1] [FSMB/p4/¶4] [Chou/p122/c2/¶2]

Tips for facilitating the referral process include:

•Do not delay in referring patients, as doing so can waste valuable time [Fishman/p68/1]

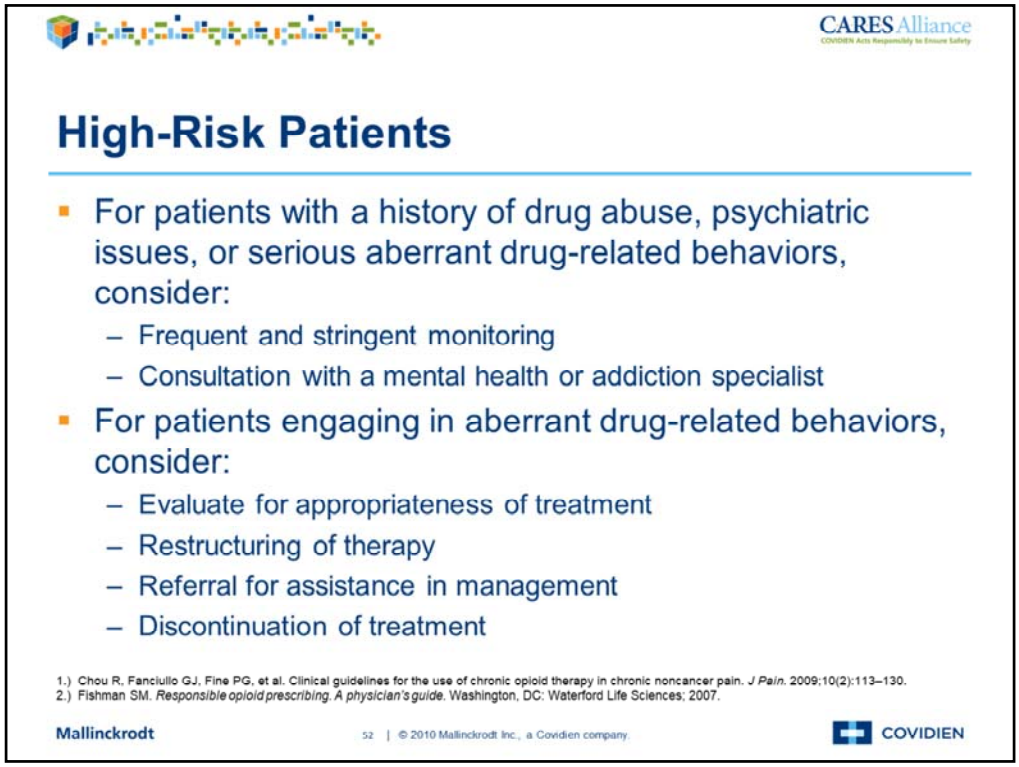
•Facilitate the referral process by obtaining the information the consultant will need to evaluate the patient [Fishman/p68/2]

•Make the referral as specific as possible by explaining just how the consultant can help you and your patient [Fishman/p68-69/3]

•Maintain a current list of colleagues who may serve as consultants when the need arises [Fishman/p69/4]

•Have a "go-to" pain specialist and addiction specialist to whom you can refer patients at the ready [Fishman/p69/5]

•Communicate with consultants so you know what they're doing to help your patient [Fishman/p69/6]



A common comorbidity among patients receiving opioid therapy is addiction and substance abuse disorder. Chronic noncancer pain occurs in patients who have a history of drug abuse and those who are at high risk for aberrant drug-related behaviors, and these patients are as equally entitled to effective pain management as patients who are at lower risk for opioid abuse, addiction, or misuse. [Chou/p119/c1/6.1+6.2] [Gourlay/p108/c1/¶3+4] [FSMB/p2/¶6]

It is recognized, however, that prescribing opioids to high-risk patients poses a clinical challenge. [Chou/p119/c1/¶3]

The following tips for HCPs may help balance the risk-benefit profile by enabling the potential benefits of opioid therapy to outweigh the potential risks in high-risk patients: [Chou/p119/c2/¶1–3;p120/c1/¶1]] [Fishman/p73-74/¶2–#3;p74/#4–6;p75/¶1-#7]

1) More frequent and intense monitoring

2) Authorization of limited prescription quantities

3) Consultation or comanagement with specialists in addiction medicine and mental health

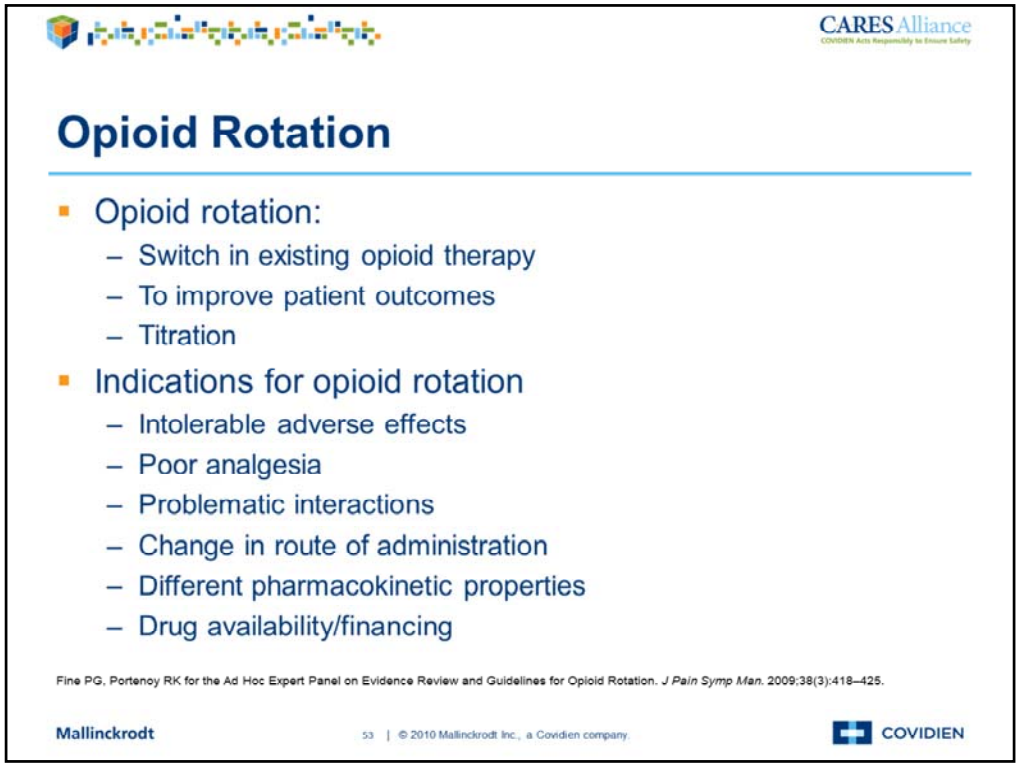
4) Re-evaluation and possible restructuring of therapy

5) Temporary or permanent tapering of opioid doses

6) Addition of psychological therapy or other nonopioid treatment, including referral for opioid detoxification and withdrawal management

7) Structured opioid agonist therapy with methadone or buprenorphine

8) Discontinuation in patients known to be diverting opioids or engaging in seriously aberrant behaviors such as injecting oral formulations



Opioid rotation, or a switch in the existing opioid therapy, is when an opioid analgesic or route of administration is changed with the goal of improving patient outcomes. [Fine/p418/c2/¶1;p419/c2/¶3+Bullets 1-3]

Indications for opioid rotation (switch in the existing opioid therapy):

•Occurrence of intolerable adverse effects during dose titration

•Poor analgesic efficacy despite aggressive dose titration

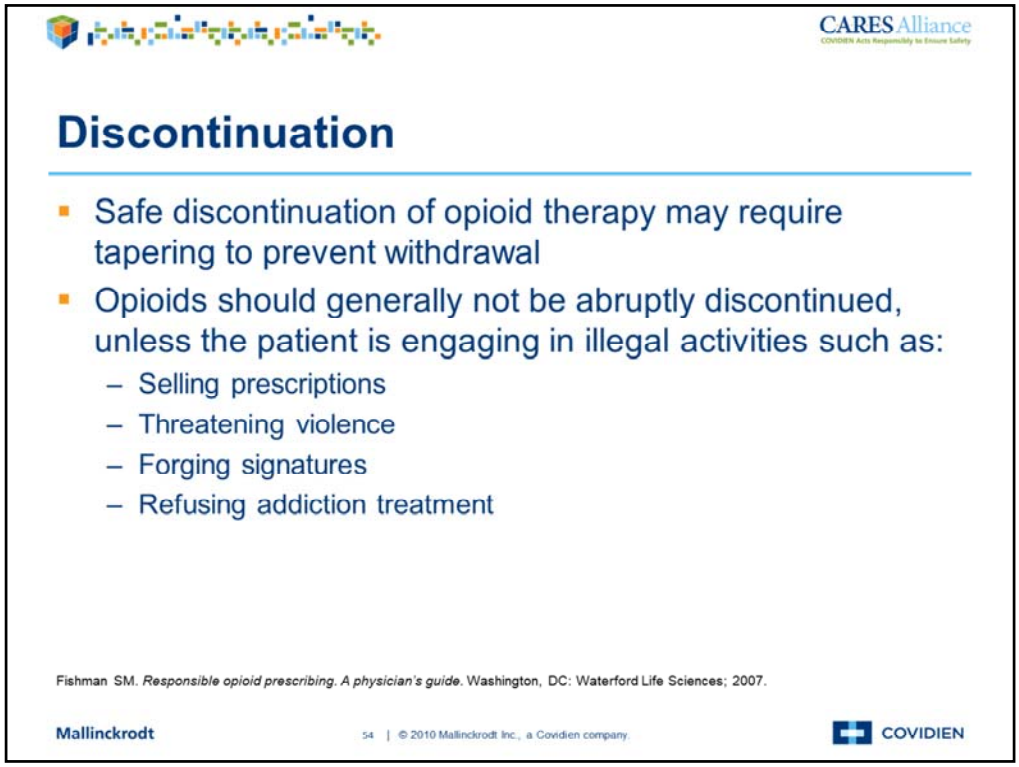
•Problematic drug-drug interactions

•Preference or need for a different route of administration

•Change in clinical status (eg, concern about drug abuse or the development of malabsorption syndrome) or clinical setting that suggests benefit from an opioid with different pharmacokinetic properties

•Financial or drug availability considerations

When rotating opioids, switching begins with selection of a starting dose that is safe and reasonably effective. [Fine/p418/c2/¶2] The starting dose of the new opioid should be based on an informed estimate of the difference in potency between the current and the new opioid, to minimize adverse effects and maintain efficacy during the switch. [Fine/p419/c1/¶1] After initiation, the new opioid dose should be individualized via titration and management of adverse effects. [Fine/p419/c1/¶1]



At times, the HCP's only option is the discontinuation of treatment.

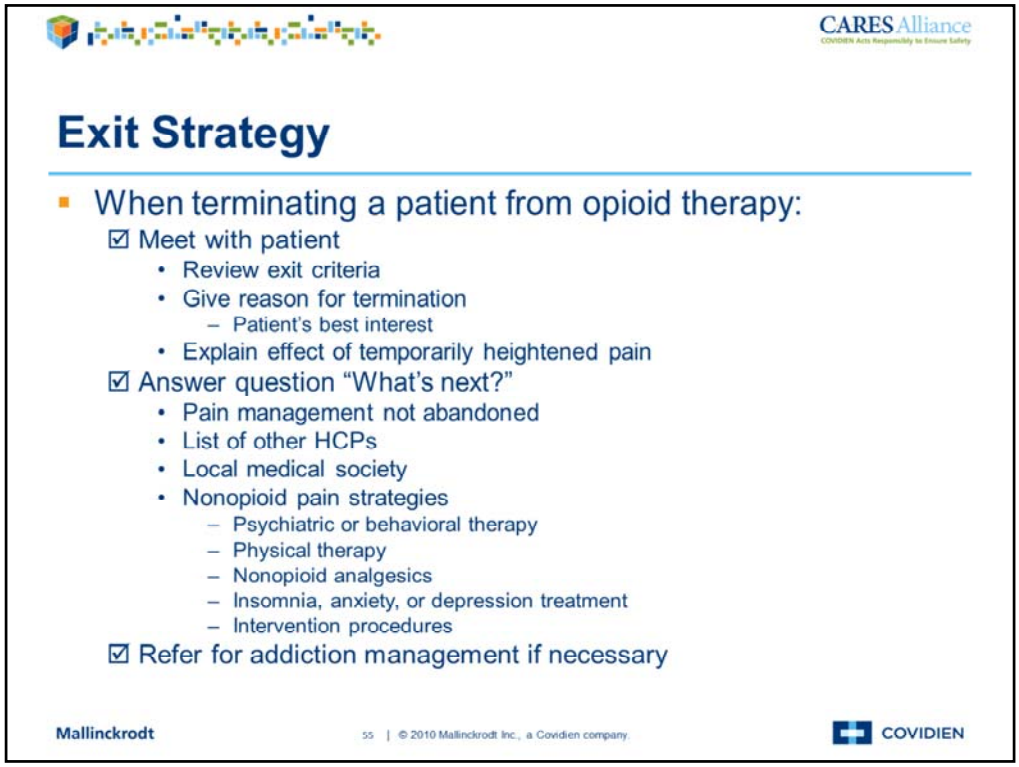
Safe discontinuation of opioid therapy requires gradual tapering of the opioid dose to prevent signs and symptoms of withdrawal in physically dependent patients. (Fishman 2007)

In general, opioid analgesics should not be abruptly discontinued. Safe discontinuation of opioid therapy may require gradual tapering of the opioid dose. [EXALGO PI/p1/c2/Bullet 6] [Embeda PI/p3/c1/¶1] [Opana PI/p11/¶3] [Oxycontin PI/p14/¶3] [Duragesic PI/p3/c2/¶6] [Fishman/p77/¶1]

When a patient is involved in illegal activity such as selling prescriptions, threatening violence, or forging signatures to obtain prescriptions, that patient should be terminated immediately. [Fishman/p76/¶2]

Termination should also be considered for patients with opioid addiction who refuse treatment for their addiction. [Fishman/p76/¶2]

Some states may have specific legal or regulatory requirements for termination of which HCPs must be aware. [Fishman/p77/¶1]



The patient should not be abandoned.

When terminating a patient from opioid therapy:

•Meet with the patient to review the exit criteria agreed upon in the treatment agreement and inform them of the reason for termination

•Clarify that termination is for the patient's benefit

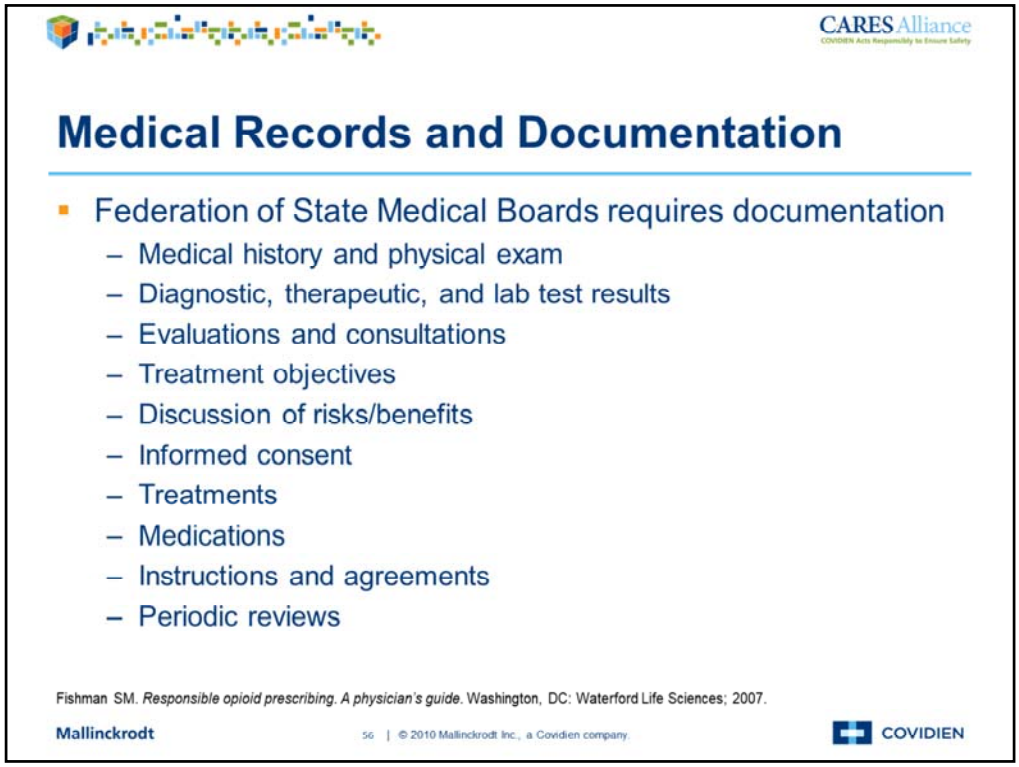
•Clarify that pain management is not being abandoned

•Provide a list of names of other HCPs in the area or information to contact the local medical society to aid them in obtaining a list of HCPs

•Explain effect of temporarily heightened pain to the patient

•Implement nonopioid pain strategies such as psychiatric or behavioral therapy, physical therapy, nonopioid analgesics, treatment for insomnia, anxiety, or depression, and interventional procedures

•For patients with apparent addiction, refer for addiction management

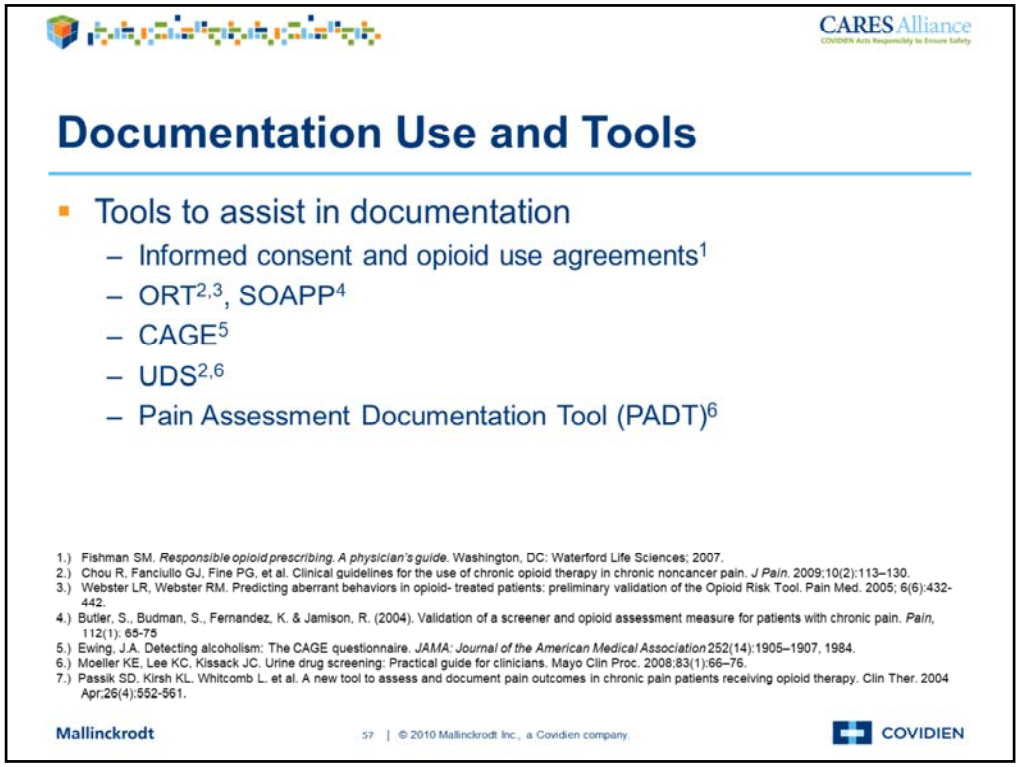


Documentation is a key aspect of monitoring, and it is a regulation HCPs must abide by. The Federation of State Medical Boards recognizes that the use of controlled substances including opioids may be necessary for the treatment of chronic pain, that the use of opioids for other than legitimate medical purposes poses a threat to individuals and to society, and that inappropriate prescribing can lead to drug misuse, abuse, and diversion. [FSMB/p3/¶2+3]

The Board therefore expects HCPs to incorporate safeguards to minimize the potential for misuse, abuse, and diversion into their practices, and all opioid prescribing must be based on clear documentation of unrelieved pain. [FSMB/p3/¶4]

Records should be kept current and accessible at all times, and should include: [FSMB/p4/¶5+#1–10] [Fishman/p81/¶3]

- Medical history and physical examination
- Results of diagnostic, therapeutic, and laboratory tests
- Evaluations and consultations
- Treatment objectives
- Discussion of treatment risks and benefits
- Informed consent
- Treatments
- Medications (including date, type, dosage, and quantity prescribed)
- Instructions and agreements
- Periodic reviews



Along with following regulatory requirements, documentation may be the best way to spot trends over time, including: progress toward treatment goals, severity of side effects, or changes in patient demeanor.

Computerized systems are available, making information more accessible, but written documentation can still be sufficient. [Fishman 2007/p81/¶1+2]

Other tools that are available to assist in documentation, include;

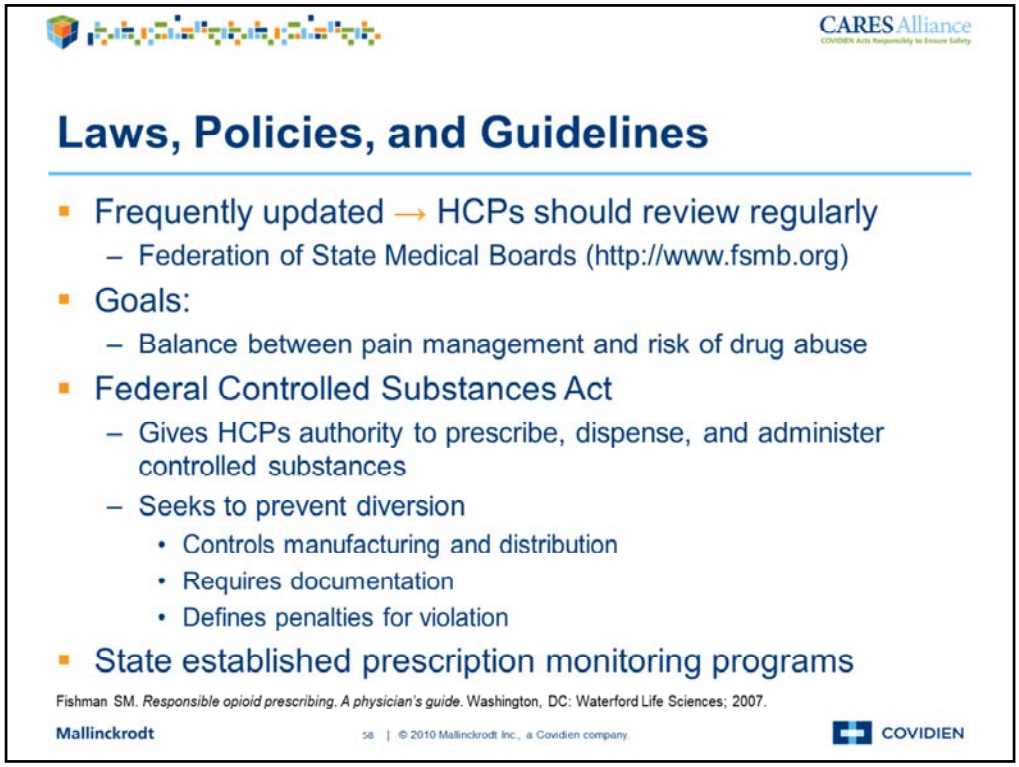
•Informed consent and opioid use agreements [Fishman/p45/¶2]

•The ORT, SOAPP, and SOAPP-R tools to assess the potential for opioid abuse [Chou/p116/c1/¶4;c2/¶2]

•The CAGE screening tool for identifying the presence of abuse [Fishman/p23/¶3]

•UDS to monitor patient adherence to opioid therapy [Chou/p118/c1–2/5.1+5.2]

•The Pain Assessment Documentation Tool (PADT) to assess treatment progress [Passik/p78/¶1+2;p79/¶1+2]



Policies and laws that guide the treatment of chronic pain and are designed to enhance pain management are frequently updated and, therefore, should be reviewed by HCPs regularly.[Fishman 2007]

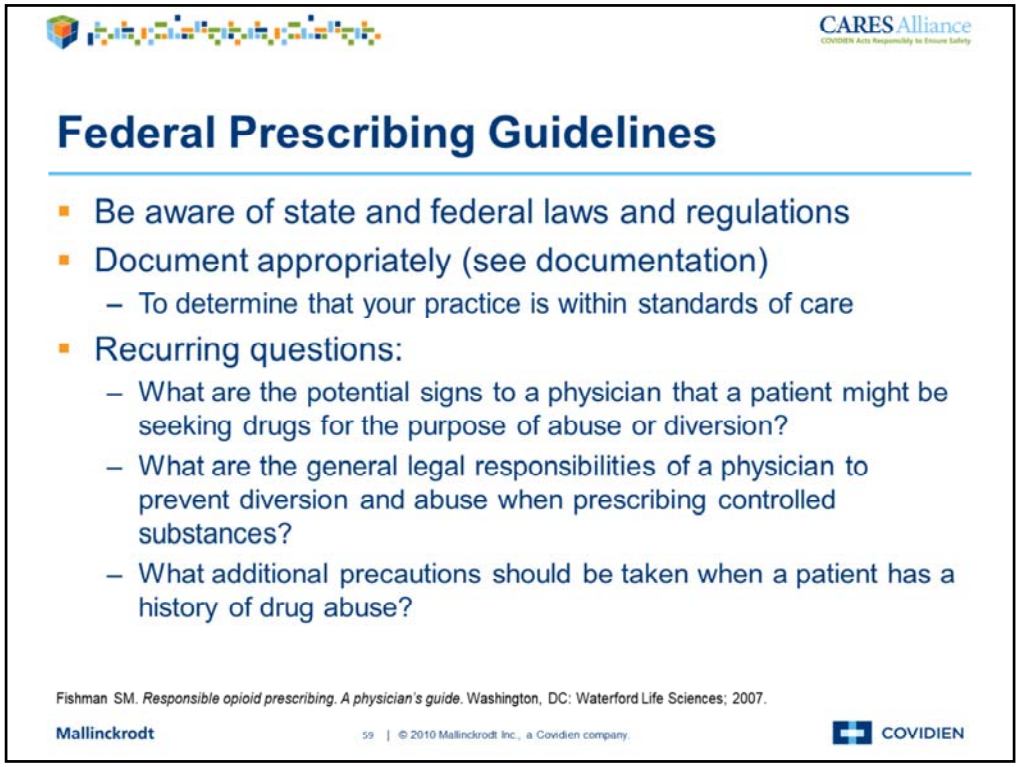
The goals of these laws, policies, and guidelines are to achieve a rational balance between a patient's right to effective pain management and society's need to be protected from drug abuse. [Fishman 2007]

Information on applicable laws guiding opioid prescribing and use can be accessed via the Federation of State Medical Boards website (http://www.fsmb.org). [Fishman 2007] , 18

HCPs who prescribe opioids must also be familiar with the Federal Controlled Substances Act (CSA), which gives authority to HCPs to prescribe, dispense, and administer controlled substances for legitimate medical purposes in the course of professional medicine. [Fishman 2007]

The CSA also seeks to prevent diversion of controlled substances by controlling manufacturing and distribution, requiring documentation, and defining penalties for violation. [Fishman 2007]

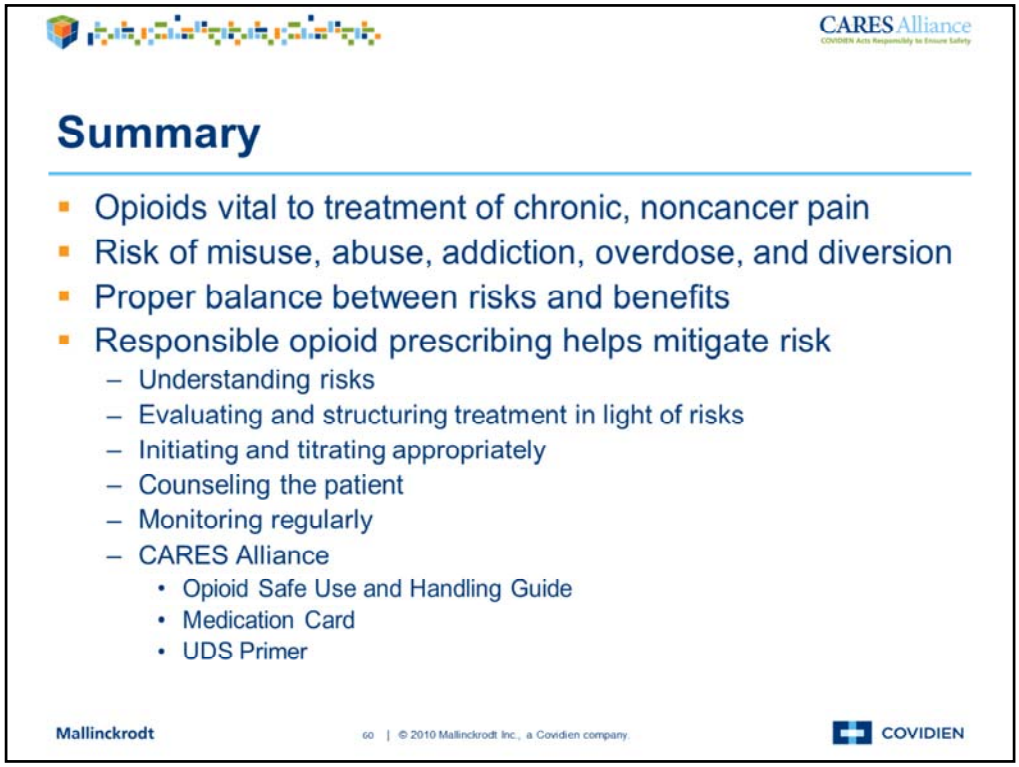
In addition, many states have established prescription monitoring programs to further address the problems of opioid diversion and abuse. [Fishman 2007]



In fall 2007, the US Drug Enforcement Agency issued a final rule allowing practitioners to provide individual patients with multiple prescriptions to be filled sequentially.

Allows for up to 90 day supply.

The interval is up to the prescriber.



Opioid analgesics are a vital component of an effective strategy for the management of chronic noncancer pain. However, opioid analgesics are not appropriate for all patients.

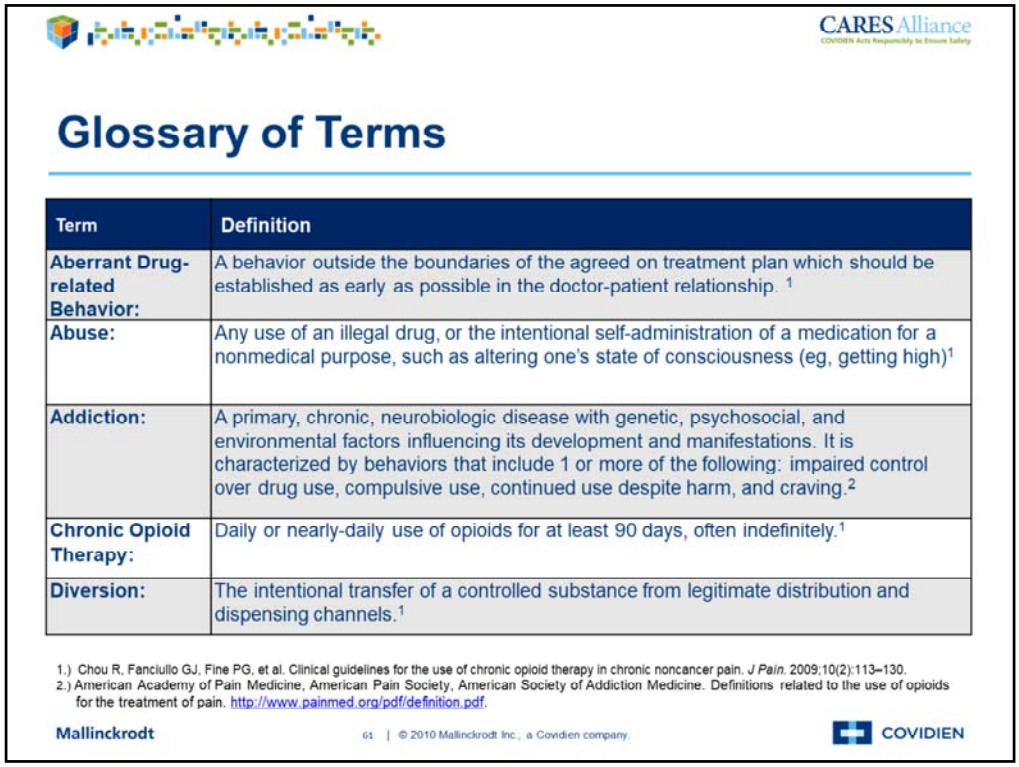
The potential for misuse, abuse, addiction, overdose, and diversion, both among patients to whom opioids are prescribed for legitimate medical purposes and among individuals who primarily obtain the medication either willfully or by theft from patients to whom they are prescribed for legitimate medical purposes, is a responsibility of the HCP.

HCPs who prescribe opioid analgesics must balance the risks of opioid therapy with the potential therapeutic benefits of these agents, and be knowledgeable in assessing and managing the risks associated with opioid therapy. With such knowledge, and by consistently and routinely employing responsible opioid prescribing and management practices, HCPs can help to mitigate the risks and optimize the benefits of opioid analgesics to improve outcomes for their patients with chronic noncancer pain. Responsible management consists of the following facets:

1) Understanding risks
2) Evaluating and structuring treatment
3) Initiating and titrating appropriately
4) Counseling the patient
5) Monitoring regularly

For additional information on responsible opioid prescribing and safe use, please consult these other CARES Alliance resources:

1) Opioid Safe use and Handling Guide for Patients
2) Medication Card
3) Urine Drug Testing Monograph
4) UDS Primer



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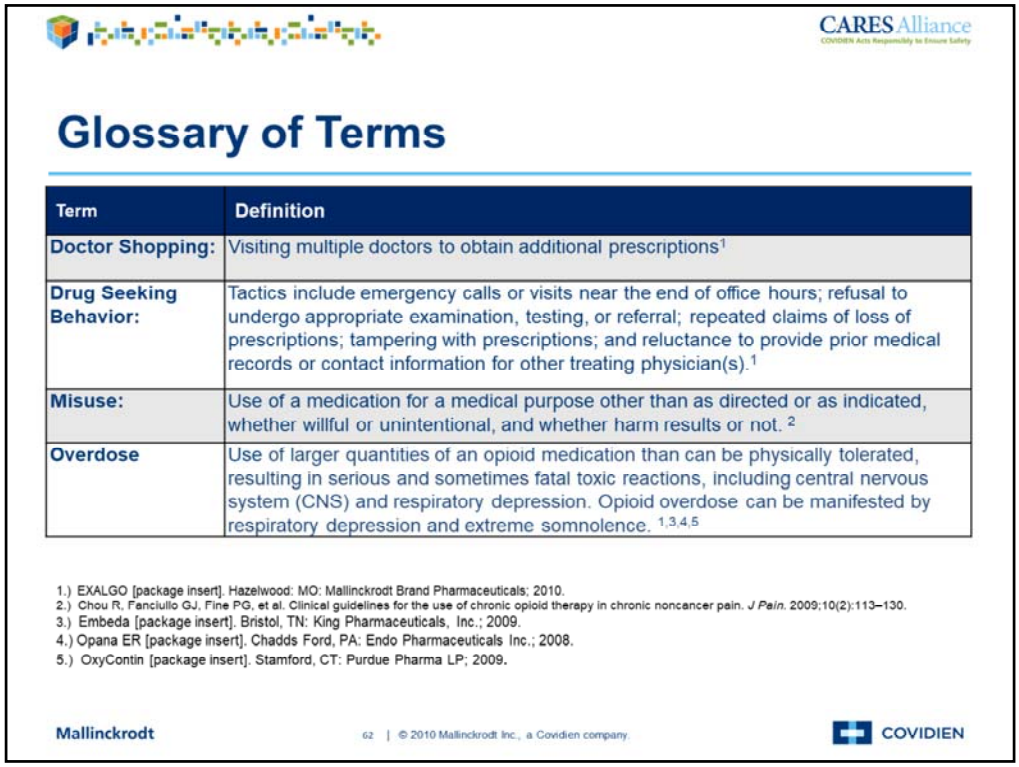
Glossary of Terms

Term	Definition
Aberrant Drug-related Behavior:	A behavior outside the boundaries of the agreed on treatment plan which should be established as early as possible in the doctor-patient relationship. [1]
Abuse:	Any use of an illegal drug, or the intentional self-administration of a medication for a nonmedical purpose, such as altering one's state of consciousness (eg, getting high)[1]
Addiction:	A primary, chronic, neurobiologic disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include 1 or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.[2]
Chronic Opioid Therapy:	Daily or nearly-daily use of opioids for at least 90 days, often indefinitely.[1]
Diversion:	The intentional transfer of a controlled substance from legitimate distribution and dispensing channels.[1]

1.) Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009;10(2):113–130.
2.) American Academy of Pain Medicine, American Pain Society, American Society of Addiction Medicine. Definitions related to the use of opioids for the treatment of pain. http://www.painmed.org/pdf/definition.pdf.



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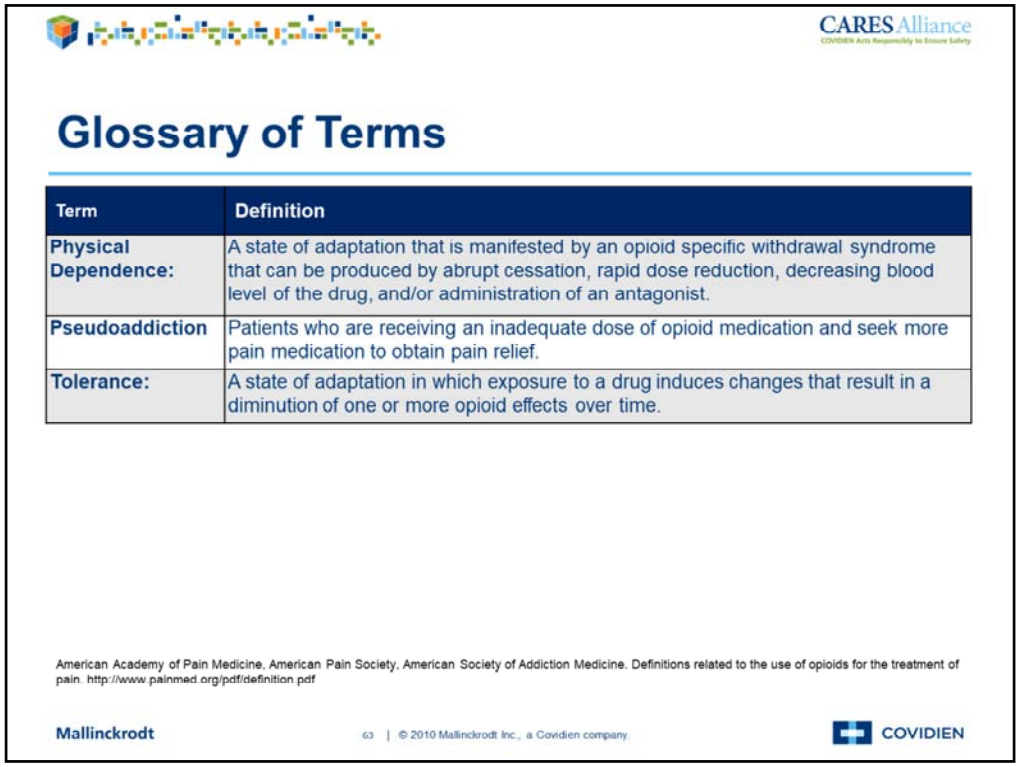
Glossary of Terms

Term	Definition
Doctor Shopping:	Visiting multiple doctors to obtain additional prescriptions[1]
Drug Seeking Behavior:	Tactics include emergency calls or visits near the end of office hours; refusal to undergo appropriate examination, testing, or referral; repeated claims of loss of prescriptions; tampering with prescriptions; and reluctance to provide prior medical records or contact information for other treating physician(s).[1]
Misuse:	Use of a medication for a medical purpose other than as directed or as indicated, whether willful or unintentional, and whether harm results or not. [2]
Overdose	Use of larger quantities of an opioid medication than can be physically tolerated, resulting in serious and sometimes fatal toxic reactions, including central nervous system (CNS) and respiratory depression. Opioid overdose can be manifested by respiratory depression and extreme somnolence. [1,3,4,5]

1.) EXALGO [package insert]. Hazelwood: MO: Mallinckrodt Brand Pharmaceuticals; 2010.
2.) Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009;10(2):113–130.
3.) Embeda [package insert]. Bristol, TN: King Pharmaceuticals, Inc.; 2009.
4.) Opana ER [package insert]. Chadds Ford, PA: Endo Pharmaceuticals Inc.; 2008.
5.) OxyContin [package insert]. Stamford, CT: Purdue Pharma LP; 2009.



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Glossary of Terms

Term	Definition
Physical Dependence:	A state of adaptation that is manifested by an opioid specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.
Pseudoaddiction	Patients who are receiving an inadequate dose of opioid medication and seek more pain medication to obtain pain relief.
Tolerance:	A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more opioid effects over time.

American Academy of Pain Medicine, American Pain Society, American Society of Addiction Medicine. Definitions related to the use of opioids for the treatment of pain. http://www.painmed.org/pdf/definition.pdf

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